PUBLIC HEALTH REPORTS

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Drs. Wiley, Alsberg, and Browne were chiefs of the Bureau of Chemistry, Department of Agriculture, and administered the Federal food and drug programs before the Food and Drug Administration was created in 1927. The others shown served as heads of the new Federal agency. See special section, pages 557–603.

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PUBLIC HEALTH REPORTS

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U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

MARION B. FOLSOM, *Secretary*

PUBLIC HEALTH SERVICE

LEONARD A. SCHEELE, *Surgeon General*

Service Statistics in Public Health

THE RENAISSANCE of interest among public health administrators in the planning and evaluation of public health programs highlights the importance of the work currently being done by the Public Health Conference on Records and Statistics.

Within the past three decades, a number of approaches have been made to the description of health department performance and the impact of public health programs. Outstanding results of these efforts are the several editions of appraisal forms for local health work issued by the Committee on Administrative Practice of the American Public Health Association, the tabulation of health department services prepared by the Committee on Records and Reports of the Conference of State and Territorial Health Officers, and, more recently, the Evaluation Schedule and Health Practice Indices developed by the Committee on Administrative Practice of the American Public Health Association. Successively, these several reporting instruments have been valuable tools for the use of local health departments in reviewing their operations. They have stimulated critical self-appraisal, an essential to growth and improvement of service.

As stock-taking techniques have been more widely applied, deficiencies in available operational statistics have become increasingly apparent. The volume of statistical information accumulated has steadily increased; yet much of it has been collected without specific purpose and, therefore, has been of minimum worth. Frequently, it is limited to enumeration of units of service, with no link to any sort of population base from which to measure program progress. For example, immunizations of various types, given at specified places, within designated periods of time, are customarily counted, but they are not related to the number of children of different age groups who should be immunized. Also, it is usual to maintain figures on attendance at the several kinds of health department clinics but unusual to relate such attendance to the number of persons who needed the service provided. Statistics kept in far too many health departments are susceptible to gross tabulations only, not to the kind of analysis necessary for pinpointing problems of specific age, socioeconomic, or geographic groups, or for measuring success or failure in meeting them.

Working Group on Service Programs

While counts of certain acts of the health department staff describe the efforts being expended for each separate program, they give no indication of what has happened as a result of the service. Although a number of health departments have recently revised their systems of compiling service statistics, no widespread agreement has been reached regarding the kind of statistical information that is most essential for the planning, operation, and evaluation of public health programs. Neither has there been any generally accepted guidance concerning the minimum amount of such information required and the kinds of breakdowns or relationships which are apt to be most generally useful.

It is to such problems that the Working Group on Service Programs—one of six working groups of the Public Health Conference on Records and Statistics—has addressed itself. The Working Group on Service Programs, until 1954 known as the Working Group on Service Statistics, is interested in data that describe and measure public health services to individuals and efforts to reduce environmental

hazards. Problems of registration and legislation pertaining to vital events are being considered by the other working groups of the conference—the working groups on (*a*) marriage and divorce, (*b*) methodology, (*c*) model legislation, (*d*) mortality, and (*e*) natality and fetal death.

The Public Health Conference on Records and Statistics was established in 1949 for the development and improvement of public health records and statistics. Membership of the conference is made up of representatives of vital and public health statistics programs of each State and Territory. The National Office of Vital Statistics serves as secretariat to the conference, and representatives of Federal and voluntary health agencies and of schools of public health participate in working group activities.

The several working groups engage in a year-round work program, which includes performance of basic studies, preparation of technical reports, and formulation of recommendations for consideration and action of the conference. Particularly significant to the guidance of effective public health action and measurement of progress are several documents which have been developed by the Working Group on Service Programs. These statements or guides have evolved from the experience and needs of the working group members and their colleagues from program divisions in the several health departments represented. In reaching its conclusions, the group has had continuous consultative service from professional leaders in the respective subject matter areas to which attention has been directed.

Meaningful Service Statistics

In order to make the conclusions of the working group widely available to public health workers, *Public Health Reports* is publishing the series of technical reports designed to improve the quality of public health service statistics. The first report, "Basic Principles Governing Service Statistics in Public Health," follows on p. 521. This initial document proposes a number of fundamental concepts which the Working Group on Service Programs believes are essential to the development of meaningful service statistics in public health. The principles enumerated will be useful to many health departments as criteria for determining the value of program statistics being produced currently or contemplated for the future.

Guides for application of these basic principles to two specific types of health programs have also been completed. Entitled "Health Supervision of Infants and Preschool Children" and "Health Services for Children of School Age," they will be published in subsequent issues. As similar guides are developed for additional program areas and are approved by the conference for publication, they too will be released through *Public Health Reports*. A guide for home accident prevention programs is nearly completed.

These statements are in no sense an attempt to standardize either content or procedures in the development of service statistics. Prescribing specific statistical patterns which would be applicable to all health departments is neither desirable nor possible. On the other hand, a sound, widely accepted framework within which each health department may develop a program in accordance with its own particular needs and resources is badly needed for more effective program planning, operation, and evaluation. The conference believes this series of guides will contribute to that end and that each statement merits extensive study and application by public health workers.

Basic Principles Governing Service Statistics in Public Health

The following principles should govern the collection, tabulation, analysis, and interpretation of service statistics:

Principle 1

Service statistics should serve one or more of these purposes:

Help define the health problems of the community.

Help measure extent of the program.

Help measure progress in relation to problems.

Help furnish a basis for future program planning.

Help provide data required periodically by the general public, local appropriating bodies, and State and Federal health agencies contributing financial aid.

Principle 2

Information accumulated for service statistics should meet the following tests:

Should be not only useful but actually used.

Should be valid.

Should be significant for the purpose it is supposed to serve.

Should be readily available.

Should justify the time and expense involved in its collection.

Report of the Working Group on Service Programs, essentially as approved April 27–29, 1955, by the Public Health Conference on Records and Statistics, Washington, D. C.

It is recognized that accepted criteria for tests of validity and significance of certain types of information are not available at present. Establishment of such criteria is a project in itself and one which should be undertaken as early as possible in order that the importance of the utility factor could be judged against the importance of the availability factor.

Principle 3

In order to be most meaningful, service statistics should be related to baseline data. Examples are:

- Demographic information, such as population by age groups, natality, morbidity, and mortality information.
- Information regarding the housing, sanitation, nutritional, and general economic status of the community.
- Health needs of special groups.
- Information describing health facilities, services, and personnel available, under public, voluntary, and private auspices.
- Information reflecting expenditures.

Definite provision should be made for correlating baseline data with the service statistics accumulated. Too frequently, while the several bodies of information are available, there is no organized method by which they are brought together.

Principle 4

The most important concept concerning service statistics is that such statistics should, generally speaking, measure services directed to individuals and their environmental hazards, including results attained, and not attempt to measure staff activities.

Major emphasis should be placed on the number of persons served and types and amount of service received, and not on numbers of visits and inspections made or other such measures of volume of staff activities.

Principle 5

In general, activity counts should not be used for service statistics.

The gravest criticism of utilizing activity counts for service statistics is the fact that a false sense of accomplishment may be engendered in health department personnel. When so many activities are recorded, there is severe temptation to think that every minute of the working time should be tabulated as evidence that full time and attention have been accorded the job. This leads to the desire to account for every letter answered, telephone call made, and even the time spent in preparing the activities report itself.

For example, items such as meetings attended as a part of duty, newspaper articles prepared, hours spent working on records, conferences with clerical personnel, attendance at professional meetings, special meetings attended, and similar activities may have administrative value to the supervisor or the program director in evaluating the distribution of staff activities, but they do not contribute directly to the measurement or evaluation of program services.

Likewise, the effectiveness of an educational program cannot be measured by number of pamphlets distributed, films shown, talks given, and so forth. Attendance at a meeting or carrying away of literature may have no relation whatsoever to what the individual learned through contact with the health information.

These questionable types of service statistics, enumerating the multitude of activities of health personnel, arise from attempts to get quantitative indexes of how much is being done in this or that program. However, mere counts of activities, without being related to the need or unmet demand for a service, add very little to knowledge of the problem or to program planning.

For example, the important thing to know in connection with immunization is the level of immunization in the community. Counting up the number of immunizations given at specified places falls far short of giving that essential knowledge.

For measuring the amount of work done, gross counts will be meaningful only for activities expressed in standard work units, such as tuberculin tests, X-rays, clinic hours held, sputum examinations, and the like. For such activities as medical consultations, medical social work, or nursing visits, they will not be meaningful unless the content of the service is specified.

For supervision, counts of activity may be useful where work can be measured on a production basis, such as laboratory examinations made or X-ray film taken. On the other hand, when work to be evaluated is of such nature that it cannot be described in easily measurable work units, this type of information lacks validity since many factors besides numbers of activities participated in are important. A mere count of activities performed reveals neither the quality of service rendered, the time required, nor the results obtained.

For informational and budgetary purposes, such counts of activities have little meaning unless expressed in terms of progress toward a goal and of comparison with known needs and with standards for service. For determining relative emphasis placed on different segments of the program, enumeration of activities is revealing only for those parts of the program which are comparable.

As an example, a count of nursing visits or admissions for two programs cannot be considered a valid comparison of relative emphasis if one program consists of clinic and home nursing services and the other is carried out through home nursing visits alone.

The more valuable service statistics—those measuring services to individuals and the improvement of their physical environment—are based on counts of the patient load according to whatever breakdowns are significant (age, sex, race, residence, and so forth) and to the categories and amount of service received, grouped so that service is related to problem. Such data are needed for both program planning and evaluation.

For example, more useful information on

maternity services can be obtained by relating antepartum, delivery, and postpartum services to the women who were delivered within a specified period than by getting unrelated counts of the three types of services.

Shown below is a pattern which relates service statistics for a tuberculosis screening activity to the problem, specifically, the number screened to the population concerned:

Total population screened.
Percentage of population screened.
Number of persons screened.
Number of films read.
Number of persons referred for large X-ray.
Number receiving large X-ray.
Number referred to physician.
Number of referrals completed.
Number diagnosed as active.

By such relationship of information, the number for whom rechecks were recommended, the percentage of individuals tested who had evidence of a disease, and the number confirmed by private physicians provide a guide to the validity of the test. The number for whom rechecks were recommended and completed is an indication of the adequacy of followup. Reporting on this basis makes possible good comparison of services between various areas and between selected periods of time.

Principle 6

Unduplicated counts of individuals receiving service is useful information to local health departments.

"Unduplicated counts of individuals" means counting only once, for a designated period of time, each separate health department client irrespective of the number and variety of health department services he receives. It is possible that a person receives more than one service from the department. In considering total volume of service given by the health agency, such a person would be counted several times. For some purposes this is desirable and important information. However, in planning, operating, and evaluating a public health program, it is also important to know the number and characteristics of each individual served by the health department. Consequently, arrangements should also be made for counting only once each person served by the health agency. In this connection, it is also important to know where the remainder of the community received comparable services, if any. These data can then be related to the population concerned and thus assist in measuring the extent to which public health effort is reaching all the people.

Principle 7

Service statistics as here discussed should, for the most part, be a byproduct of administrative operation of a program.

Maintenance of records and compilation and interpretation of statistics should be an integral part of program management. Case records of individuals served by the health department constitute the best source of service data in a well-conducted department.

Principle 8

To promote the use of selected information from case records, the basic record system should be so designed that pertinent items can be related without the necessity of searching through scattered sources.

The record being used should permit easy recording and review of the information it contains. One possibility of achieving this end is a single case record for each client, on which is recorded all types of service rendered by the health department. The record should also be readily accessible for review after it is filed. Such a record system must be worked out within the circumstances of individual health departments.

Principle 9

A review of the service record for each individual under health department supervision should be made regularly, at least annually, by the supervising staff.

Case record analysis can be limited to stated times: quarterly, semiannually, or annually. Periodic review reduces handling and permits

more thorough analysis. Such a review would require for each individual service:

- A plan.
- The existence of standard criteria of service (nursing, clinic, medical, social, rehabilitation, and so forth).
- A comparison of performance as revealed in the record against the plan and the criteria of service.

Periodic review of each individual service record would provide valuable leads to evaluation of the adequacy of health department service. An accumulation of unmet needs would reveal where emphasis should be put and would indicate needs for and distribution of personnel.

For example, if an analysis is made once a year of all known tuberculosis cases to determine how many tuberculosis patients are in the hospital, how many at home, the sputum status of those at home, and the number of tuberculous individuals at home who were last examined more than a year ago, attention is focused on a specific problem and on the health department's success, or lack of it, in keeping individuals under supervision.

If, in addition, records of all new tuberculosis cases are examined to determine the stage of the disease, and the age of the patient, attention will be drawn to the success of case finding.

A summary of this type of data provides appropriating bodies with a better understanding of the health department program and its needs than does the traditional count of visits, inspections, and admissions to broad categories of service. It is recognized that information from records needs to be supplemented by personal observations and knowledge of the person doing the job.

Periodic case record analysis would be less expensive and more valuable than the accumulation of a vast quantity of uninterpreted data, which is still a wide practice among public health agencies.

While compilation of service statistics by periodic case record analysis has been initiated in several places, it has not been extensively developed. Even when such types of data are collected, the resulting tabulations are too frequently not used and are not coordinated with operation of the program.

Review procedures should provide a mechanism for closing out the records of individuals no longer needing service or for determining priority of those needing service.

Principle 10

In order that only pertinent data be collected and that there be no duplication either of effort or data, health departments should have a committee for the development, review, and control of basic records, forms, and procedures.

In State health departments, the committee described above should include at least the director of local health services and representatives of the statistical unit, selected programs, and local health department. At either the State level or the local level, personnel who actually use records and interpret procedures should participate in their design and assist in establishing procedures for their use.

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The basic principles have been reproduced in mimeographed form as Document 353 of the Public Health Conference on Records and Statistics by the National Office of Vital Statistics, Public Health Service, Department of Health, Education, and Welfare, Washington 25, D. C. They have the endorsement of the following organizations: Association of State and Territorial Directors of Local Health Services; Council of State Directors of Public Health Nursing; Statistics Section and Committee on Administrative Practice, American Public Health Association.

Conference Report

Evaluation in Public Health

THE First National Conference on Evaluation in Public Health evolved from a need for pooling the experience of the many individuals and groups concerned with evaluation of public health activities and stimulating the development of more effective evaluative techniques. Dr. Vlado A. Getting, professor of public health practice, School of Public Health, University of Michigan, was chairman of the planning committee. He opened the conference by stating its two main objectives: to bring together the work of many in the evaluation of public health so that all may profit; and to determine which steps logically might be taken next to improve the practice of evaluation of public health activities.

Background

Indirectly, the conference was an outgrowth of a recommendation made in 1953 by the Association of State and Territorial Health Officers:

"That a joint committee be established, representing the Public Health Service, Children's Bureau, and the Association of State and Territorial Health Officers, to develop quantitative and qualitative measurements which could be used to evaluate public health programs."

More immediately, it resulted from a meeting called in Buffalo, N. Y., on October 10, 1954, by the chairman of the association's representatives to the joint committee, Dr. J. D. Porterfield, director of the Ohio State Department of Mental Hygiene and Correction. In addition to the representatives of the Federal agencies and the State health officers, there were representatives from several organizations, which had planned or initiated studies concerned with evaluation of public health activities.

A planning committee was appointed to convene a 2-day working conference to learn more of what each group is doing and to develop a cooperative plan in which the various individual contributions could be dovetailed for the maximum contribution to the development of quantitative and qualitative measurement in public health practice.

Membership of the planning committee comprised representatives of the American Public Health Association, the Association of Business Management in Public Health, the Association of State and Territorial Health Officers, and the Children's Bureau and Public Health Service of the Department of Health, Education, and Welfare. These five agencies, in cooperation with the University of Michigan School of Public Health, sponsored the First National Conference on Evaluation in Public Health.

Structure

The conference was designed to enable the participants to discuss methods of evaluation as they applied to one of five specific health activities. A maximum of 20 persons participated in the discussions of each section. Participants were selected on the basis of their demonstrated interest in evaluation, and they were chosen from a wide range of professional

The First National Conference on Evaluation in Public Health was held at the School of Public Health, University of Michigan, September 12 and 13, 1955. This summary of the recommendations of the conference and some of its discussions was prepared by the Division of General Health Services, Bureau of State Services, Public Health Service, at the request of the conference's planning committee.

disciplines: medicine, nursing, engineering, dentistry, sociology, administration, and psychology.

The plenary orientation session was followed by simultaneous sessions of the five sections. Section discussions were related to selected specific programs: tuberculosis control, fluoridation of water supplies, accident prevention, prematurity, and cancer control. These specific topics encouraged the consideration of concrete examples of methodology. Discussions were aimed at bringing out the component processes of evaluation which might, or might not, be common to other public health practices.

Digests of the section discussions were summarized by a resolving committee chaired by Dr. Herman E. Hilleboe, commissioner of health of New York State. The committee's summary report was presented at the final plenary session for discussion and action by the entire conference.

Planning—Anderson

The keynote address for the conference was delivered by Dr. Otis L. Anderson, chief of the Bureau of State Services, Public Health Service, whose formal topic was planning in relation to evaluation.

Dr. Anderson posed two basic tenets: first, that planning for the evaluation of a program should be interwoven with planning for the program itself; second, that evaluation techniques should be applied in the improvement of planning.

He enumerated the several successive phases of program planning, viewed in its broadest sense, as follows:

1. Determination of specific problems or needs.

2. Delineation of long-term and short-term goals or objectives.

3. Assessment of resources available or obtainable, including public opinion, professional attitudes, and degree of cooperation which might be expected; funds; personnel; facilities; technical knowledge, and so forth.

4. Selection of program methods or activities to be used to gain objectives.

5. Continuous or periodic evaluation of achievement or progress toward attainment of short-term and long-term goals—both quantitative, or measurable, and qualitative, or judicious appraisals.

6. Change in goals, redirection of program, or replanning, as indicated by accomplishment, by concurrent shifts in circumstances, improvements in useful knowledge, and altered resources.

7. Evaluation of final results.

Built-In Evaluation

In this pattern of program planning, the speaker explained that evaluation is built right into the plan as an identified, integral part. Evaluation cannot be considered an adjunct to public health program development, to be pursued or omitted as convenience dictates. It must be involved as an essential ingredient of of program design, serving a definite purpose. Dr. Anderson demonstrated the application of this concept to a number of specific programs.

Every phase of positive program planning contains an element of evaluation, he said. Assessment and judgment are involved, and decisions must be made whether we are determining the extent of a problem, public opinion, resources available, or completeness of technical knowledge or whether we are establishing objectives or choosing methods for action geared to achieving the objectives. Each decision depends upon considering and choosing among alternatives. This weighing of evidence throughout the planning process is an informal, almost subconscious type of evaluation—but evaluation, nonetheless. Often, by careful analysis, it is possible to identify important related facts of which we had not been aware, thus "firming up" a base for our decisions.

Only when evaluation is built in as one dimension of program planning will it assure that proper provision has been made for validly appraising the success or failure of the program and that there is guidance for reconsideration of objectives and redirection of program, as such changes are indicated. Through prompt adjustment of program, much effort and expense that otherwise might be wasted can be saved. Available resources can be rechanneled without delay into more productive and more needed activities. Unless this is done, the program plan becomes static and sterile, and

completely valueless as an administrative tool.

For any program, Dr. Anderson said, there is a better chance of achieving long-range objectives if planning provides for progress evaluation of intermediate steps and of objectives at frequent intervals. Such evaluation yields immediate results. Concurrent evaluations make it possible to identify difficulties or barriers as they occur and to apply necessary adjustments.

On the other hand, if evaluation is delayed until objectives are achieved, the program may never be evaluated. Or if the appraisal is arbitrarily timed—in conection with a reorganization or a change in administration—we may find that for a long time we have been engaging in fruitless endeavor, and that the advance in measurable program achievement, the end and aim of program planning, has not been accomplished.

Need of Evaluation—Kandle

Dr. Roscoe P. Kandle, deputy commissioner of health of New York City, talking on the need and place of evaluation in public health, urged that a fresh start be made in the evaluation of public health practices, with renewed ambition and new perspectives. The public health profession is now on "dead center" with respect to evaluation in public health, he stated.

He praised the work of past years by the Committee on Administrative Practice of the American Public Health Association, supported by the Commonwealth Fund and by other groups, in developing various methods of appraisal and evaluation of specific public health techniques. He also noted outstanding current work, such as that in evaluating several methods of tuberculosis control, in pinpointing specific causes of infant mortality and in appraising the effectiveness of efforts to reduce these problems, in carrying out precise studies of diagnostic tests and practices for control of coronary disease and hypertension, and in developing new methods and formulas for determining the number of public health nurses needed for adequate service to a community.

Nevertheless, the evaluation of widely used public health practices remains a major weakness, Dr. Kandle stated. Growth of programs has outstripped our ability and ambition for appraisal. He directed attention to several barriers which have not been penetrated successfully:

1. There is a strong tendency to think of effort rather than of accomplishment. There are not many practical indexes of accomplishment.

2. There is a lack of true perception and precise knowledge of people's actions and beliefs about health and the changes we are trying to encourage them to make. To evaluate without taking into account the factors of the people's understandings and feelings is foolish and wasteful.

3. It is difficult to devise simple, practical evaluation procedures which can be built into everyday practice.

4. We are apt to conform too rigidly to narrow public health traditions. This produces stereotyped thinking, which limits critical, incisive analysis of our accomplishments and fresh and original approaches to our problems.

Report of Resolving Committee—Hilleboe

The extent to which the conference attained its objectives is reflected in the summary report of the Resolving Committee which was presented by Dr. Hilleboe.

Dr. Hilleboe reported that he found many similar opinions among the representatives of the five sections. He emphasized that when evaluation in public health is discussed, there must be understanding about what is to be accomplished. Accordingly, a program is needed. We also must have a plan of operation which is, of course, based on the program plan. If we evaluate what we are doing in the light of what we set out to do, then we are moving in the right direction, he said.

We can evaluate a technique, a research project, a study, an activity, an objective, a purpose, or a total program, Dr. Hilleboe continued. We need to evaluate the yardsticks, the tools of measurement, themselves. It is also true that we can do some administrative evaluation, and its importance in carrying out all of our public health programs should not be forgotten. We can evaluate both performance and measures of performance; ultimately, we must evaluate performance against our stated objectives.

This basic principle came out time and again in many of the sectional discussions, Dr. Hilleboe reported. Highlights of the rest of his report included the following:

It is possible to become so absorbed in one particular technique that an undue amount of time is spent in evaluating that single technique. Sooner or later we must determine the value of the technique to the activity in which it is used. The activity in turn must be related to objectives, and they, in turn, to the purpose of the entire program.

Evaluation in public health becomes meaningful when it originates from a critical attitude of mind and intellectual curiosity. Those are fundamental ingredients. Program evaluation requires the same meticulous skills and methodology that the epidemiologist employs in the study of an acute or chronic disease. It is not enough to make measurements; what is needed is the measurement of results. Reliable and valid techniques can produce measurable results if expertly used. Precise evaluation studies are really research projects of one kind or another, and are quite similar, in fact, to the epidemiological field studies made by health department personnel. Both use the scientific method to obtain unbiased results.

The evaluation process should employ scientific measurement and comparison in public health practice as in other fields. Certainly the public health profession should use a scientific method whether it is in administration, or the evaluation of a technique, or the activities or programs that make up the substance of public health. Evaluation studies to be sound require appropriate samples.

In evaluating techniques, reliability, validity, yield, cost, and acceptance, must be measured. But when objectives and programs are considered, the factors of adequacy and efficiency must be added to our evaluation. Cost must be taken into account because all program plans depend upon money for continued operation. It is essential to determine if the evaluation is going to be worth the time, effort, and money spent in relation to the limited resources available for all health department work.

The human factor must be recognized in the evaluation process. Suggested changes in program content and direction may threaten the security of the individuals concerned, so evaluation must consider human relations in public health.

The several sections of the conference are in general agreement. One of the strong currents running throughout the whole discussion was the feeling that there is considerable value in exchanging ideas and experiences on evaluation, that the conference has been profitable, and that constructive, definite recommendations resulted.

It appears that the initial need is to have a small group, perhaps taken from this conference, start work on developing acceptable and unified terminology and definitions. This will enable public health people to communicate with each other more easily and precisely and to talk more profitably about evaluation.

Many of the health organizations represented here, both public and private, can look at some of their programs to see if some new evaluation projects can be set up. Within the next 12 months some evaluation projects could be started where they have not been carried on before. Every full-time health unit can begin some evaluation work even if it is only the testing of a minor technique or administrative procedure. It is up to us to find the resources within our own departments and do something in evaluation that we haven't done before. Then we can communicate with one another and exchange information of mutual benefit.

There should be another conference of this type, in about a year, to which all of us can bring the results of our new evaluation projects for open discussion. Prior to the proposed conference, copies of reports of projects can be distributed so that criticism and discussions of these evaluation projects may be more concentrated when we do convene. This would lead naturally to still further evaluation.

From our intense discussions of the past 2 days have come principles and practices in evaluation which can be useful to many health workers throughout the world. To set up a clearinghouse on evaluation in public health would be a natural followup, one which would enable all to keep abreast of present and future development in this field. It would provide for continuous exchange of experience and other information, and duplication of effort in pur-

suing the same types of evaluation might be avoided. Thus we would get the greatest benefits possible out of the human effort and the monetary expense involved.

Such a course of action may well herald a new and exciting era for public health in a changing world.

Conference Action—Witmer

Discussion of the Resolving Committee's report was opened by Dr. Helen L. Witmer, director of research, Children's Bureau, Department of Health, Education, and Welfare, who emphasized that difficulty in keeping on a straight track in planning for program evaluation arises from the fact that programs are so complex. She likened them to social institutions which, she said, can easily be divided into their component parts: purpose or objectives; personnel and clientele; rules—legal, ethical, technical (instruments, procedures, techniques); and equipment—facilities, including money activities.

One of two pertinent questions might then be asked regarding each element:

1. Is it scientifically valid? (Does the kind of staff, equipment, and procedures used lead to the desired results?) or

2. Is it good (the staff or the results) according to accepted standards?

Ideally, standards should be based on scientific validation. When this is not possible they must be based on judgment and experience. The main thing in planning and carrying out evaluation is clarity of purpose and direction.

Most of the audience discussion pertained to the recommendations proposed by the Resolving Committee. The final action of the conference was the adoption of the following recommendations:

Copies of the full Proceedings of the First National Conference on Evaluation in Public Health may be purchased from the University Publications Distribution Service, 311 Maynard Street, Ann Arbor, Mich.

The clearinghouse function recommended by the conference has been delegated to the Subcommittee on State and Local Health Administration of the Committee on Administrative Practice of the American Public Health Association. Forms for registration of projects may be obtained from Dr. Vlado A. Getting, chairman of the subcommittee, whose address is School of Public Health, University of Michigan, Ann Arbor, Mich.

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1. That a small group be designated to develop uniform, acceptable terminology for general use in public health evaluation. (This recommendation was prompted by the fact that all groups reported that confusion concerning terminology had characterized and hindered their discussions.)

2. That each health agency represented start some evaluation project within the next 12 months and carefully document the methodology used.

3. That another conference be held within one year for the purpose of reviewing the projects and determining methods and techniques which could be used by other agencies.

4. That a clearinghouse be established for continuous exchange of experience and prevention of duplication of effort in the development of methods and criteria for evaluation.

5. That the necessary staff and financial support be obtained to set up this central agency on evaluation.

Montefiore Demonstration Project

Practical Nurse Training in the Home

By MARTIN CHERKASKY, M.D., ELIZABETH B. TORRANCE, M.A., R.N., ELSIE BANDMAN, M.A., R.N., and BETTY SEIFMAN, M.A., R.N.

THE INCREASE in chronic disease has created a host of problems. These derive not only from the mounting number of chronically ill patients, but also from the long duration of chronic disease and the associated emotional, social, and economic disorders that affect both patient and family.

The changing character of illness is shown by reports from visiting nurse agencies throughout the country that their services are devoted more and more to patients with chronic disease. The Visiting Nurse Service of New York reported that in a recent 6-month period 70 percent of the visits were to patients with long-term illness.

Because chronic illness is measured in months and even years, it has become neither desirable nor possible for all the chronically ill to be cared for in hospitals, certainly not for the major period of illness. This consideration has caused many changes in the patterns of medical care (*1*).

Montefiore Hospital, New York City, recognizing the impossibility of providing institutional facilities for all the chronically ill and the undesirability of keeping many patients in institutions rather than in the home with their families, embarked in 1947 upon its home care program. Techniques of providing comprehensive care to patients in the home were fully explored and have in many instances served as the pattern for home care programs throughout the country as well as abroad (*2*). Of particular significance throughout the United States is a growing number of organized programs of home care designed to meet the complex needs of chronically ill patients within the framework of the home (*3–9*).

It is fortunate that this necessity has considerable virtue. Montefiore has demonstrated that, for properly selected patients, home care is a method of choice when the basic team of the physician, nurse, and social worker is available to meet the multiple needs of the patient and his family. Of these three, none is more important in this service than the nurse.

The rise in chronic disease, which will assuredly continue, has led not only to a shortage of institutional facilities but to an even more serious shortage, that of nursing personnel. The American Nurses Association reported that there were 389,600 active professional workers at the end of 1953. Of these 231,000 were professional nurses employed in the field of hospital and institutional nursing. An additional 54,123 practical nurses were also employed in that field (*10*).

Although this was the largest number of professional nurses who had ever practiced in the country, the demand has kept well ahead of the supply. One of the reasons for this demand is the enormous growth of hospital facilities. In 1934 the total number of hospital beds in this

Dr. Cherkasky is director, and Miss Torrance is nursing executive, of Montefiore Hospital in New York City. Miss Bandman, formerly supervisor of the hospital's demonstration project for practical nurse training in the home, is now assistant nursing executive of the hospital's School of Practical Nursing. Miss Seifman succeeded Miss Bandman as supervisor of the demonstration project.

country, excluding those for the mentally sick and tuberculous, was 464,193, and in 1953 it was 735,215 (*11*).

In 1940, hospitals pressed by the growing demand of the armed forces for nursing personnel further developed a new hospital worker—the trained practical nurse. Today, patient care would be impossible in many of our hospitals were it not for the trained practical nurse, at first accepted only grudgingly by her colleagues and others in the health field. Her period of training, in contrast to the minimum 3 years for the professional registered nurse, is approximately 1 year. To qualify for practical nurse training at Montefiore Hospital, the student must have certain qualifications:

Age: 17–50.

Education: Elementary school diploma or its equivalent.

Health: Applicant must have good physical and mental health and moral character. Medical and dental records must be filled out by the applicant's own physician and dentist on a form provided by the school.

Selection: An admissions committee makes the final selection, based upon an evaluation of the applicant by personal interview, preentrance testing, and references.

Obviously the pretraining qualifications and the length and extent of training preclude the average practical nurse from assuming the same range of responsibility as the professional nurse. There is, however, no question that, with proper selection of students and a year of carefully planned and supervised training, the practical nurse is prepared for a wide range of nursing services which supplement and complement the services of the professional nurse.

In view of the great problem of chronic disease and the growth of home care programs, it is inevitable that a considerable part of the burden of nursing care in the home, as well as in the hospital, will have to be carried by the trained practical nurse.

The Questions

In 1952, Montefiore Hospital approached the New York Foundation with a request that it support a 2-year research program designed to answer the following questions:

Without major changes in the length of the curriculum, what are the functions and services which the practical nurse is best prepared to carry out for the sick person in the home? What is the role of the practical nurse in the home on her own; as a member of an organized home care team; or as a member of a visiting nurse service? How much of the training year should be devoted to training in the home? What should be the nature of the training in the home? In addition to training in the home, what changes are desirable in the basic curriculum of practical nurse training which will enable her to do the best job in the care of the sick at home? What is the cost of such a program?

One of the conditions making our situation particularly suitable for this practical nurse demonstration was the close and vital relationship that had been built up in the preceding 5 years between the Montefiore department of home care and the Visiting Nurse Service of New York, the agency under contract for service to Montefiore home care patients (*12*). A VNS supervisor has also acted as nursing consultant to the program.

With an extensive experience in chronic disease, with a home care program carrying an average census of about 85 patients, with a well-established school of practical nursing, with a close tie to the Visiting Nurse Service, and, above all, with the philosophy of the team approach to the care of the chronically sick, the Montefiore Hospital division of social medicine was chosen for this project.

Program Description

The study was scheduled for October 1, 1952, to October 1, 1954. A full-time supervisor was employed for student orientation, teaching, and general administration of the study. And a contractual agreement was drawn up to cover the care of patients under the joint service of the hospital and the Visiting Nurse Service of New York.

During the 2-year period, 159 students in the Montefiore School of Practical Nursing received a 3-week period of training in the home of patients after basic work in medical and surgical nursing. The average number of stu-

Table 1. Average student day [1] in home training project

Activity	Percent	Hours
Total	100	8
Time spent with patient	37	3
Travel	25	2
Clinical instruction	12	1
Home care conference and seminar	6	½
Formal class	10	¾
Recording	10	¾

[1] Does not include lunch.

dents in the program at any given time was six.

A typical period will be of value in presenting some of the activities in the home. During the 6 months, January 1 to June 25, 1954, there were 8 training classes consisting of a total of 35 students who each received a 3-week course in home care. Table 1 shows the average student day during home training and table 2, the activities during the period.

The transition between work in the hospital wards in which a student practical nurse was assigned to limited responsibility for a specific patient to the increased responsibility for a patient in his home presented an educational challenge.

An orientation course of several hours was given to each student on her first day and was continued for as many successive days as needed. This course included statements explaining the philosophy of the home care department, its team approach, and its many patient care functions. The aims and services of the Visiting Nurse Service of New York, as well as the cooperative agreement between the pilot study program and the Visiting Nurse Service, were discussed. Presented in detail were the specific responsibilities of the student to the patient as well as her relationship to the supervisor and to the physician. Modified procedures, such as home methods for sterilizing instruments and thermometers, were demonstrated. Approach to the patient, entry into the home, and attitude and concern for environmental deficiencies were explained. Finally, the individual patient, his physical ailments, and his emotional and social needs were discussed preparatory to the student's initial visit.

Table 2. Visits to patients, nursing hours, and services of 35 students, Jan. 1 to June 25, 1954

Item	Number
Visits to patients	724
Total hours	1,025
Services performed for patients	10,137
General care	3,767
Treatments (including physical therapy and occupational therapy)	1,189
Medications	273
Food and nutrition	601
Homemaking	359
Recording	1,522
Assisting doctor	24
Conferences	853
Miscellaneous (including diversion and encouragement of patient)	1,549

Throughout the experience, the student participated in, and contributed to, home care team conferences. Introductory visits to the patient were made jointly by the student and the visiting nurse. At this time, the student could observe the visiting nurse's approach to the patient and her procedures. This made subsequent contacts between the student and the patient more satisfactory. Followup visits were under the guidance of the pilot study supervisor until the student exhibited mastery of a given activity. Students also visited patients with home care physicians, occupational therapists, and physiotherapists, and observed a variety of advanced procedures ranging from thoracentesis to massage and exercise. They observed the staff's interchange of information, which had as its objective improved service to the patient and the family. In the home, students performed a variety of nursing procedures as well as essential homemaking activities.

The Answers

What is the role of the practical nurse in the home?

The practical nurse demonstrated during this study that she was competent and efficient in a patient's home. She was capable of performing a variety of nursing procedures ranging from a simple bath to sterile dressings, care of tracheotomy patients, administration of oxygen, and preparation of food for patients on regular and special diets. She was able to make necessary and frequently complex adjustments

of basic skills to meet individual needs in the home.

The practical nurse student, through her training in the home and family setting, developed appreciation of the patient as an individual and of the importance of family relationships in the care of the sick. Each succeeding visit increased her insight and her sensitivity to the emotional stresses and medical, nursing, and socioeconomic problems of her patient.

In a teamwork setting, the student learned the role of the physician and social worker and developed a clear understanding of her own function not only as a practical nurse, but also as a participant in the team. Personal contact between staff members and the practical nurse student fostered mutual respect and understanding. As a member of the Visiting Nurse Service team, she proved her value in effectively relieving the professional nurse of certain routine bedside nursing duties in a manner that was highly acceptable to the patient.

It is, however, important to remember that a 1-year period of training, no matter how excellent, is not designed to give the practical nurse opportunity to learn the many nursing procedures that the professional nurse studies in 3 years.

The advice of Marian G. Randall, executive director of the Visiting Nurse Service of New York, is pertinent: "Continue the excellent plan of teaching patient-centered nursing but give the student the added security of teaching her what she should not do in the home on her own, and of teaching her the signs and symptoms which indicate when she should ask for help and supervision. In the hospital there is always someone near, but in the home the nurse is without professional assistance and there is need to recognize the difference."

Preferably, the practical nurse after her year of training should work within the framework of an agency, such as a visiting nurse service, so that under supervision she may gradually assume greater responsibility in the home.

The Visiting Nurse Service of New York, for instance, employed three of the practical nurse graduates who had received home training, waiving on a trial basis the prerequisite of 1 year of graduate experience. After the VNS supervisor became convinced of their capacity, the practical nurse graduates administered intramuscular injections to selected patients in addition to other duties.

How much of the training year should be devoted to training in the home?

At the outset and on a trial basis, we allocated 3 weeks of the curriculum for the home nursing experience. The first week was devoted largely to student orientation to the program. The program as a whole was discussed, case load assigned, travel directions given, patient care given, patients' case histories studied, and diagnostic signs and symptoms discussed. It was during this first week, too, that the student made, with the visiting nurse, an introductory visit to each of her patients.

The second and third weeks were devoted to assigned case loads under fairly constant supervision of the program supervisor. During this period the various problems that arose were discussed, case studies were written, and examinations given and corrected.

As we gained experience, the faculty concluded that despite a tight curriculum a home training program extended to 4 weeks would provide a broader learning experience. The student could be given more opportunity for independent practice, with supervision as required, and a longer period in which to develop initiative, resourcefulness, and judgment. The supervisor would have more time to evaluate the student's strengths and needs.

What is the nature of the training in the home?

Observations. The student practical nurse observed the visiting nurse giving care, which included subcutaneous injections and dressings. This was followed by the supervisor's discussion of principles involved in giving care.

Discussion and demonstration. The supervisor demonstrated modifications of procedures such as boiling instruments and cleaning thermometers. She then had the student demonstrate her grasp of these techniques. The visiting nurse shared with the practical nurse student some of the ingenious methods devised over the years which enabled her to work effectively in the home, such as: (*a*) care of equipment; (*b*)

improvised equipment, for example, bed rest and tray made out of cartons; slippers and wastebags made out of newspapers; paper padding in lieu of rubber sheeting.

Formal class teaching. Reading was assigned to students. Class discussion was held on specific illnesses and their signs, symptoms, and medication, all correlated to particular patients. Examinations were given, corrected, and reviewed with the students on an individual as well as a group basis.

Each student was assigned a particular pa tient for whom a written patient-care study was required. These patient-care studies were discussed and evaluated.

Conferences and seminars. The student attended the weekly home care conferences where patients were discussed. The students were free to ask questions. Frequently, a student's patient-care study was used as the basis for discussion at such a conference.

A 2-hour conference was held with each group of students and the occupational therapist. Here, the purpose of occupational therapy and patient suitability for occupational therapy were discussed. In turn, the students frequently called to the attention of the occupational therapist patients who seemed in need of such therapy.

At an orientation conference with the social worker, the students received further insight into understanding the patient as a person and a family member.

Scheduled informal conferences were held by the physical therapist with the students following home visits.

Homemaking duties. Homemaking duties, generally, were minimal. The student was primarily responsible for cleaning the bedside unit.

Since diet and preparation of food are included in the curriculum, the student was familiar with various types of diet, such as bland and salt-free. The program supervisor discussed in detail with each student the dietary requirements of her patients. She stressed the help the nurse could give the patient in understanding and continuing a diet which, while therapeutic, was sometimes quite unpleasant. Whenever necessary, the student prepared and served a patient's food and did other minor household chores. It is interesting and significant that the practical nurse student was unenthusiastic about duties which were specifically homemaking.

What are the necessary curriculum changes?

The home care experience has resulted in a major reorientation of our curriculum. Not only has it improved the training of practical nurses so that they can function adequately in the home, but it also has sharpened our understanding of the kind of curriculum we require to train a practical nurse to function better in all responsibilities. Heretofore, the curriculum had been focused on mastery of subject matter and nursing procedures as isolated factual material. Even before the pilot study, the need for a patient-centered curriculum had begun to be apparent. In the pilot study, it became quite clear the student was having difficulty in integrating her learning and adapting it to each patient.

The first change was in the content and technique of presenting the more than 70 hours of "conditions of illness." Instead of teaching the major disease entities, the focus was shifted toward the patient with a disease in need of nursing care. All pertinent information relating to the disease—its etiology, symptoms, and treatment, including drugs and diet—was reviewed in the light of its contribution to effective nursing care. The patient's emotional needs and the devastating social effect of long-term illness also were integrated into the teaching program. Advanced nursing procedures, such as thoracentesis, paracentesis, and lumbar puncture, have been included in the conditions of illness course within their appropriate context, rather than presenting them as part of the nursing arts course. Ward conferences, including allied health personnel, revolving around a student's nursing plan for a specific patient have been helpful in training the patient-oriented nurse.

This orientation of the student nurse to the patient may seem so natural and right as to raise the question why it was not done before. Of course, in some measure it always has been done. The problem faced in nursing education parallels that of medical education. The focus of our teaching is so sharply directed toward

the multiplicity of facts and techniques our students must learn that we tend to forget the primary purpose of nursing education, which is care of the patient. It has been said that the technician has become both so skilled and so narrow that he knows everything about his job but its purpose. It is imperative that the attention of the student nurse be directed as positively to the entire patient as to any group of specific skills. Seeing patients as people and within a family setting is one of the best ways of accomplishing this purpose.

The second deficiency, that of lack of adequate information in the biological areas, has been remedied by another shift in the curriculum. This involved reducing the number of hours allocated to the domestic arts and the hygiene courses and increasing the allocation of hours spent on body structure and function and drugs and solutions.

Our concern with the curriculum is not ended, and it is expected that many more revisions will be made.

Cost of Program

The cost of the 2-year demonstration of home training for student practical nurses was $16,293. A breakdown of the expenditures follows:

Personnel	$11,300.65
Salaries	10,662.98
Perquisites	442.92
Social Security	194.75
Student expense	2,411.94
Transportation	1,492.83
Lunches	887.71
Telephone	31.40
Other expenses	1,189.17
Travel	161.02
Consumable supplies	828.15
Statistical service	200.00
Miscellaneous and overhead	1,392.14
Total expenditures	$16,293.90

While it cost about $8,000 a year to conduct this project on an experimental basis, it is likely that, as a routine part of a school for practical nursing, the same program could be conducted for no more than $7,000 a year. This is encouraging since it seems quite obvious that the additional cost of including home care in the curriculum will be within the means of most schools. It must be recognized, however, that one of the reasons for the relative inexpensiveness of this additional teaching activity was the presence of a well-organized home care program and a well-organized and cooperative visiting nurse service.

Conclusions

1. The practical nurse, with proper preparation during her training, can contribute effectively to the growing responsibility for care of patients in the home.

2. The practical nurse, with proper delineation of responsibilities, can supplement and complement the professional nurse.

3. To insure that the practical nurse is prepared for what will inevitably be her responsibility for care in the home (as well as in the hospital), the curriculum for her student training should be primarily patient-oriented. We feel this should include a 4-week period of training in the home, preferably within the framework of a well-organized home care program.

4. The sensitivity, compassion, and understanding, which are the hallmarks of the superior nurse, are not the result of training alone. In many instances, a practical nurse, properly prepared, can bring these attributes to the patient in the home or in the hospital, particularly if she is accepted as a member of the team along with the doctor, the social worker, and the professional nurse.

5. It is not difficult to insert within the curriculum the time necessary for home care, and the budgetary implications are not of such great moment as to make this financially impracticable, particularly if there is an organized program of home care and an effective and cooperating visiting nurse service. Continued experience in training practical nurses in the home and for the home should, and undoubtedly will, lead to further curriculum changes.

6. A program that brings the nursing department of a hospital and the staff of the school of practical nursing into the home has a very beneficial effect upon the attitudes and understanding of the top professional personnel. It is extremely difficult for professional workers to think about patients as whole people

in society when they are only seen in the narrow setting of an institution. Bringing the staff of the nursing school in close contact with patients, in their natural settings as members of the family in the home, cannot but favorably influence the training of the nurses in the same manner as this device is now being used to favorably influence the training of physicians (*13*).

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NOTE: *The Montefiore Hospital demonstration project, supported by a grant from the New York Foundation, is one of several programs sponsored by the National Association for Practical Nurse Education to determine the value of home care training in the practical nurse curriculum. A composite report including the experience of all the programs sponsored by the NAPNE will be published shortly.*

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Joint Services Sanitary Engineer Training Courses

The first joint training courses for reserve sanitary engineer officers of the commissioned services—Army, Navy, Air Force, and Public Health Service—were held in June 1956 at the Robert A. Taft Sanitary Engineering Center of the Public Health Service in Cincinnati.

Developed jointly by the Department of Defense and Department of Health, Education, and Welfare, in collaboration with the National Research Council, these courses are especially designed for reserve engineer officers normally on inactive status. The courses will bring them up to date on professional developments in sanitary engineering and will provide information on sanitary engineering emergency operations applicable to situations in natural disasters and in military and civil defense emergencies.

To plan an effective program for the control of gonorrhea, more understanding is needed of the clinical course of the disease, its epidemiology, and its response to treatment.

Unknowns and Enigmas in Gonorrhea

By IRA LEO SCHAMBERG, M.D.

THE dramatic reduction in the incidence of syphilis is one of the great achievements of the last decade. Since 1947, there has been a nationwide decrease of 93 percent in reported morbidity of primary and secondary syphilis (*1*). The striking reduction in the number of such patients reported from public health clinics, where morbidity reporting is most complete, as well as from private physicians, suggests that this represents a real decrease in syphilis morbidity.

Gonorrhea morbidity has not followed suit, as indicated in figures 1, 2, and 3. The purpose of this paper is to present a number of unanswered questions about this ubiquitous disease. Possibly, when some of these questions have been answered we may understand why gonorrhea is reacting so differently from syphilis to modern therapeutic and public health measures.

As Babione (*2*) stated in 1949, "The true incidence of gonorrhea in the United States is unknown and virtually unknowable." He suggested determination of the ratio of gonorrhea to syphilis, a disease for which the incidence is known with greater accuracy, as an approach to a more valid picture of the frequency of gonorrhea. In his elaborate statistical study, he computed this ratio by age in the United States Navy for 1945 and suggested that this baseline may be used in the future in estimating changes of effectiveness of control measures applied to either gonorrhea or syphilis. The increasing difference in incidence which seems to have appeared between these two diseases in recent years would appear to make this method invalid.

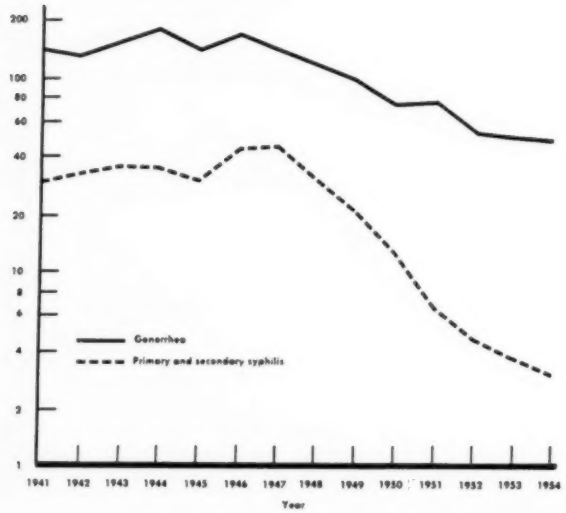
Morbidity reporting of gonorrhea among civilians has always been faulty, and conclusions drawn from such data must be made extremely cautiously. Reporting by public health clinics is a great deal more accurate than reporting by private physicians. However, patients may, for a wide variety of reasons, such as employment, economic status, or convenience, transfer from clinic to private physician or vice versa. Therefore, conclusions regarding incidence based solely on morbidity reporting from public health clinics are also open to serious error (*3*). Reporting by the armed services is, in all likelihood, more complete than reporting by civilians, but there are, nonetheless, many deficiencies. Evidence bearing on the incidence of gonorrhea in the United States may be summarized as follows:

1. Gonorrhea trend analyses have been made

Dr. Schamberg is chief, section of venereal disease control, Philadelphia Department of Public Health; assistant professor of dermatology, Graduate School of Medicine, University of Pennsylvania; and chief, department of dermatology, Albert Einstein Medical Center, Northern Division, Philadelphia, Pa.

This paper was presented at regional venereal disease control seminars in Omaha, Nebr., Atlantic City, N. J., and Miami Beach, Fla., March 9 and 23 and April 20, 1955, respectively, and at the Symposium for Recent Advances in the Study of Venereal Diseases, Washington, D. C., April 29, 1955.

Figure 1. Primary and secondary syphilis and gonorrhea in the white male, 1941–54: rates per 100,000 population, continental United States.



Source: Morbidity reports, Public Health Service.

by the Venereal Disease Program of the Public Health Service (*4*). In reviewing data on gonorrhea cases among nonwhite males reported by clinics in 13 of the larger cities of the country during the period 1952–54, it was observed that some of the cities showed no change in numbers of cases reported; some showed a moderate increase; and some, a moderate decrease. No uniform trend was noted.

2. Analysis of the gonorrhea case rate for the United States from 1919 through 1954 (*1*) shows that the case rate per 100,000 population in 1954 (152) was slightly higher than in 1919 (148). The highest incidence in 1947 (284) may have been related in part to the policy of many health departments at that time of providing the then expensive penicillin free in return for morbidity reporting of venereal disease.

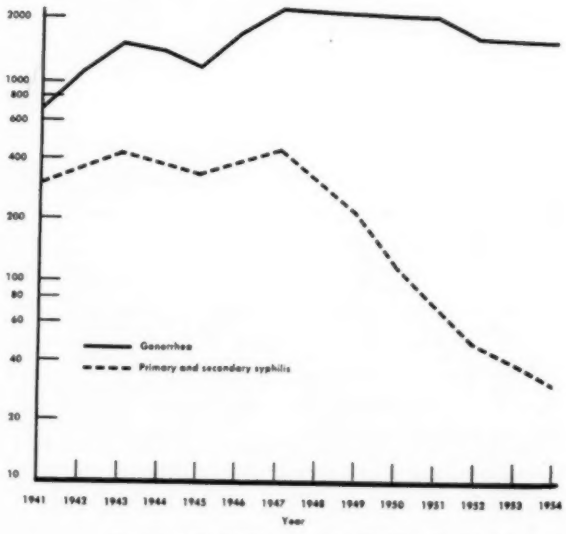
3. Review of venereal disease rates in the armed services reveals a decrease in syphilis (chiefly primary and secondary stages) in the Army of 85 percent, and an increase in gonorrhea of 11 percent from 1935 through 1953. In the Navy, syphilis decreased 98 percent, gonorrhea 70 percent (personal communication from the Surgeon Generals' offices, U. S. Army and U. S. Navy). The apparent decrease in gonorrhea in the Navy may be at least partly explained by the fact that the 1935 figure applied to the entire Navy, the 1953 figure only to naval personnel within the continental United States.

From these data, because of the factors mentioned above, we cannot know for certain whether gonorrhea has increased or decreased in incidence. However, it appears improbable that there has been a precipitous decline in incidence such as has occurred in early syphilis.

Many practicing physicians with whom the author has talked have expressed surprise that there is no evidence of a marked decrease in gonorrhea incidence. They state that they now see only a very few patients with gonorrhea, whereas in the past they saw many such patients. They add that complications of gonorrhea, such as arthritis and epididymitis, are now rarities. This widespread clinical impression may be at least partly explained on the following bases:

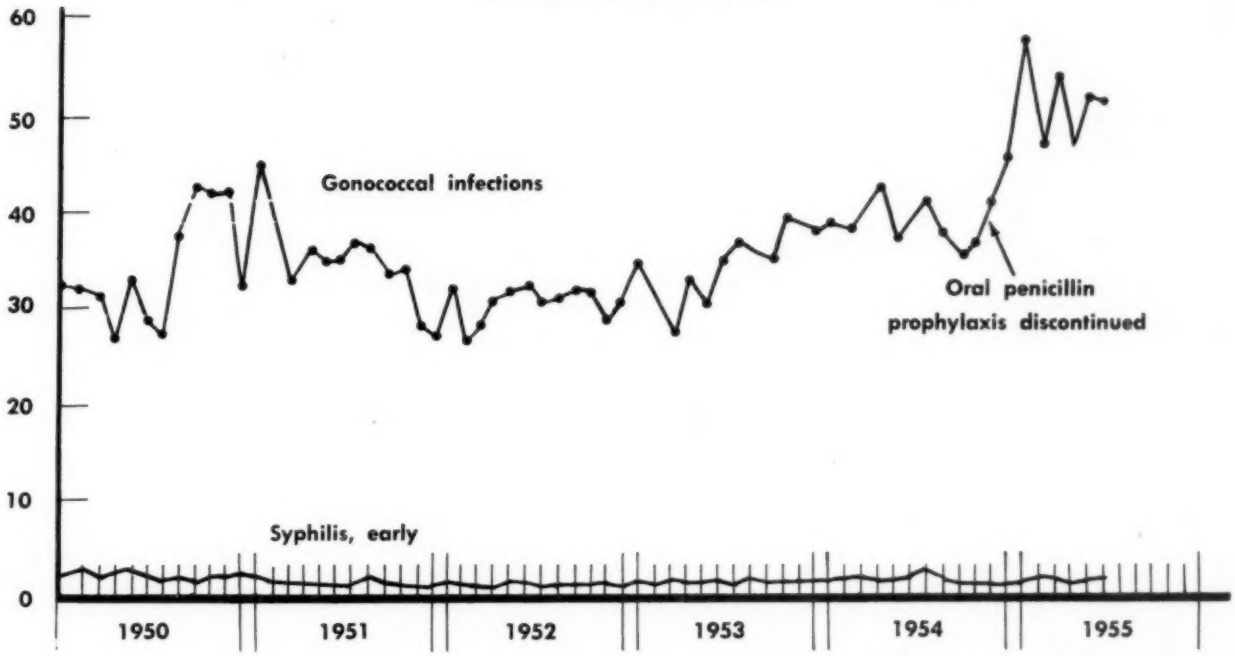
1. In the presulfonamide days (before 1937), all types of gonorrhea persisted over a period of weeks or months. If one may estimate that in those days the average male patient with gonorrhea visited a clinic or physician 3 times a week for 3 months, he would have been seen approximately 40 times. Today, the male patient with gonorrhea need be seen only once to

Figure 2. Primary and secondary syphilis and gonorrhea in the nonwhite male, 1941–54: rates per 100,000 population, continental United States.



Source: Morbidity reports, Public Health Service.

Figure 3. Syphilis and gonorrhea in United States Navy and Marine Corps, 1950–55: annual incidence rates per 1,000.



Source: Stat Navy Med July 1953 September 1955.

receive his curative injection of penicillin. This sharp decrease in the number of times patients with gonorrhea are now seen might be interpreted by the physician as a decrease in incidence.

2. Every general practitioner today is able to cure gonorrhea promptly. Therefore, many patients who previously were referred to clinics and specialists are now being seen only by the general practitioner.

3. A change in the character of gonorrhea in the course of the past 20 years may partly explain the great decrease in complications of gonorrhea.

4. Another explanation may be that the majority of individuals infected with gonorrhea are treated relatively early with penicillin, which prevents the development of complications.

It is probable that intensive public health control measures plus widespread use of penicillin for diseases other than syphilis are the factors chiefly responsible for the dramatic decline in syphilis. One would think that gonorrhea would be more susceptible to these measures than is syphilis. In the male, the incubation period is short, permitting time for infection of few sexual contacts before symptoms appear, and symptoms usually bring the patient promptly to medical care. Transmission almost solely by sexual contact limits the number of exposed individuals. Penicillin cures rapidly and makes the patient noninfectious. In addition, for the past 2 years in many areas of the country, public health measures to achieve prompt treatment of female contacts have been carried out.

On the other hand, the brief incubation period can favor the spread of gonorrhea, as has been pointed out by Magnuson in a personal communication. Penicillin given fortuitously for an unrelated condition must be given during the incubation period of gonorrhea if it is to curb infectiousness more rapidly than will penicillin given for the disease itself. It is less likely that penicillin will be received coincidentally during a brief incubation period than during a long one.

The following questions come to mind.

Q. Does penicillin cure gonorrhea?

A. Love and Finland (*5*) have recently shown that the gonococcus has not developed resistance to penicillin in vitro in the period 1945–54. However, there is evidence that some or-

ganisms are most sensitive to penicillin when actively metabolizing and are significantly more resistant when in a quiescent state (*6*). Rees (*7*) states, "When the gonococcus lies in a closed or intermittently draining focus, it may escape the action of penicillin, and is a potential source of reinfection if the focus is reopened." "Failure" of penicillin to cure gonorrhea has been reported by a number of authors (*8–13*), and may usually be explained by one of the following factors:

1. Reinfection.
2. Inadequate dosage.
3. Destruction of penicillin by penicillinase.
4. Resistance of inactive gonococci in an unfavorable environment (*6*).
5. Too brief blood level (aqueous penicillin, exertion, hyperemia of depot, low renal threshold, and so forth).
6. Misdiagnosis (nonspecific urethritis, and so forth).

Q. How long is gonorrhea infectious in the untreated female?

A. No evidence is available, in view of the impossibility of differentiating persistence of infection from reinfection.

Q. What factors cause or favor development of gonorrheal pelvic inflammatory diseases (PID)?

A. Some theories, no factual knowledge.

Q. What percentage of infected females develop PID?

A. Lewis (*14*) believes that many escape.

Q. What is the time interval from infection to PID?

A. Wertheim, as quoted by Peters (*15*), is said to have found gonococci in the endometrium 5 to 14 days after sex contact. There are many conjectures, but no knowledge.

Q. In the woman with PID does a positive cervical or urethral culture result from the original infection which caused the PID or from more recent superinfection?

A. No data, but in view of the lack of immunity resulting from gonorrheal infection and difficulty in culturing gonococci in women with PID of long duration, the latter appears probable.

Q. Is the patient with PID infectious?

A. In a study of sexual contacts of men with gonorrhea, Goldstein (*16*) found positive cervical cultures in 35 percent of the women who had PID and in only 21 percent of those found free of PID (table 1).

Q. Are women with repeatedly negative cultures necessarily free of infection and noninfectious?

A. Lewis (*14*) and Rees (*7*) believe that intermittently draining cervical glands may permit a woman to be infectious from time to time despite repeated negative cultures. The male urethra may also be a more efficient sampler and culture medium than are the physician's swab and the bacteriologist's petri dish. Koch (*17*) found, in women with gonorrheal cervicitis, alkaline cervical mucus and a high percentage of positive gonorrhea cultures in the first half of the menstrual cycle, acid cervical mucus and few positive cultures from the 22d to the 25th day (table 1). Therefore, negative cultures late in the menstrual cycle would appear to give no assurance of freedom from infection.

Q. In the female, can persistence of gonorrheal infection, relapse, reinfection, and superinfection be differentiated?

A. To date, no.

Q. Does penicillinase inactivate penicillin locally and prevent cure of gonorrheal proctitis?

A. Hagerman (*18*) found a higher relapse rate in women with proctitis and suggested that penicillinase (produced by *Bacterium coli*) inactivates penicillin in the rectum. However, Bang (*19*) found no evidence to support this thesis. Many bacteria produce penicillinase, an enzyme which destroys the antibacterial action of penicillin, and Tacking (*20*) has shown that secondary infection by one of these bacteria may inhibit the action of penicillin against pathogenic penicillin sensitive organisms in vivo.

Q. How can the effect of an intensive public health attack on gonorrhea be evaluated?

A. Greenberg and Mattison (*21*) have emphasized the importance of program evaluation and give examples of intermediate and ultimate objectives that may be used. The attack rates of urethritis in the male and of pelvic inflammatory disease in the female appear to be our best measuring rods.

Table 1. Gonorrhea cultures in women

Source of culture and author	Year	Type of patient	Number of women	Percent positive
Cervix:				
Davidson and Shepard (*32*)	1948	Named sex contacts of males with gonorrhea	42	34
Goldstein (*16*)	1955	do	538	21
Somerson et al. (*37*)	1955	do	86	47
Cohn (*28*)	1944	"Suggestive history or suspicious symptoms of GC."	230	36
Cooke and Lankford (*33*)	1945	Obstetrics and gynecology clinic	2,000	23
Morton (*37*)	1945	Young women apprehended on morals charges	over 500	about 25
Peters (*15*)	1947	Gynecology clinic	2,832	14
Koch (*17*)	1947	6–16 days postmenstrual	[1] 4	96
		22–25 days postmenstrual	[2] 4	0
Goldstein (*16*)	1955	Named sex contacts with PID [3]	49	35
Urethra:				
Cohn (*28*)	1944	"Suggestive history or suspicious symptoms of GC."	230	18
Rectum:				
Bang (*19*)	1954	"Women with gonorrhea"	428	25
Fallopian tubes:				
Menge (*34*)	1897	PID	106	22
Hyde (*34*)		do	2,973	19
Andrews (*34*)		do	634	22
Curtis (*31*)	1921	PID with gross evidence of active inflammation	64	30
		PID without gross evidence of active inflammation.	128	0
Studdiford (*35*)	1938	PID	24	67
Cohn (*28*)	1944	PID (7 treated with sulfa)	19	0
Intra-abdominal fluid:				
Vermeeren and TeLinde (*36*)	1954	Ruptured pelvic abscesses	21	0

[1] 25 cultures. [2] 16 cultures. [3] Pelvic inflammatory disease.

Q. Has the attack rate of urethritis in the male and pelvic inflammatory disease in the female been reduced?

A. No evidence has been found for a drop in PID, but Lee (*22*) has shown a decrease in urethritis in the male in a rural area adjacent to a military installation during an intensive campaign (table 2). Pereyra and his co-workers (*3*) have carried out a most interesting study in Atlanta, Ga. During an intensive 1½-year campaign, the number of nonwhite male patients applying to the health department clinic with gonorrhea has remained approximately constant. However, 15 Negro physicians practicing in the area stated on interview that they had experienced a 77-percent decrease in gonorrhea in males in their offices from 1952 through 1954. In addition, many clinic patients interviewed in 1955 stated that they had previously received treatment for gonorrhea from a private physician. The authors conclude that a shift of patients from private to clinic care conceals an actual decrease in gonorrhea incidence.

Table 2. Effect of vigorous campaign against gonorrhea in an area near a large Army camp [1]

Date	Morbidity (in males)	
	Civilian (number of cases)	Military (rate per 1,000)
January–June 1951 [2]	444	270
July–December 1951 [3]	398	201
January–June 1952 [4]	304	162

[1] Lee, S. S.: Gonorrhea control measures—A study in New Hanover County, N. C. Pub. Health Rep. 69: 998–1007, October 1954.
[2] 6 months prior to campaign.
[3] First 6 months of campaign.
[4] Second 6 months of campaign.

Q. What percentage of men sexually exposed to women with infectious gonorrhea acquire infection?

A. Certainly not all of them (personal communication from E. W. Thomas).

Q. Why do some escape?

A. May it be related to the length of the

urethra distal to the fossa navicularis? (Personal communication from P. Pelouze.)

Q. Is nongonococcal urethritis a venereal disease?

A. This condition is probably not a single entity, but in different patients may be due to mechanical, chemical, toxic, infectious, or psychosomatic factors, individually or in combination. Certain types may be transmitted by sexual intercourse.

Q. Does the gonococcus transmute into pleuropneumonia-like organisms (PPLO) under adverse conditions, and thereby become penicillin resistant?

A. Pleuropneumonia-like organisms cause certain animal diseases (bovine pleuropneumonia, agalactia in sheep and goats, polyarthritis in rats) and are found in normal humans in the female genital tract, throat, and saliva.

These organisms are resistant to all antibiotics except streptomycin.

They have been grown from cultures of eight different bacteria (including the gonococcus) when penicillin is added to solid culture media.

On transfer to fluid media, PPLO from *Streptobacillus moniliformis*, *Proteus*, and *Bacteroides* revert to original form; from other organisms, PPLO fails to grow. (PPLO isolated from animals and humans grow well in fluid media.)

Two theories may explain these phenomena: (*a*) symbiotic or accidental association of PPLO with bacteria; (*b*) growth phase—bacteria change to PPLO form under adverse conditions and thereby become penicillin resistant (*23–27*).

Q. Why is so little research in gonorrhea being carried out in this country? A search of the recent literature reveals significantly more investigative work on gonorrhea in the Scandinavian countries, Germany, Russia, and Great Britain than in the United States.

A. Reasons for this lack of research in the United States are not known.

How may we in the future learn the answers to some of these questions?

1. Better diagnostic tools might be developed, such as more sensitive cultural methods. Cohn and Grunstein (*28*) and Schauffler (personal communication) consider gonococcus culture an insensitive method, in that many organisms must be inoculated in order to get growth. Another tool would be sensitive and specific serologic, skin, or other tests.

2. Repeated examination of women in a protected environment, following natural or purposeful infection, in order to observe the natural course of the disease and response to treatment. Such studies have been carried out in syphilis (*29*) and in gonorrhea in the male (*30*), and are equally permissible, feasible, and potentially valuable in gonorrhea in the female.

3. Repeated urethral and cervical cultures from women scheduled for hysterectomy. After operation, cultures from the excised cervix utilizing the following methods and materials: micropipette aspiration of cervical glands under the dissecting microscope, scraping of multiple cut surfaces, groundup pieces of tissue, and pus and exudate. Sensitivity of cultures would be greatly enhanced under these conditions.

4. After baseline studies of untreated women, similar studies on women treated with penicillin should help to answer the question whether penicillin cures gonorrhea in the female.

5. Similar studies in women with pelvic inflammatory disease scheduled for laparotomy. In the era of surgical treatment for PID, bacteriological studies at operation provided interesting data. Curtis (*31*) in 1921 reported on bacteriological study of fallopian tubes from 192 patients. The gonococcus was found in 30 percent of tubes showing gross evidence of active inflammation but was found in no case in which the tubes were grossly negative, even when there was histological evidence of active inflammation. Curtis stated that it is only rarely possible to obtain viable gonococci from patients who have been free from fever and leucocytosis for more than 10 days to 2 weeks. He concluded that the gonococcus lives only a short time in the tube, and that persistently or recurrently active gonorrheal salpingitis is due either to recurrence of infection from without (reinfection) or to repeated invasion of bacteria from the chronically infected lower genital tract. Such studies should be repeated using the most sensitive present-day cultural methods.

Conclusions

1. The true incidence of gonorrhea in the United States is unknown.

2. Widespread use of antibiotics and intensive control measures have reduced the attack rate of syphilis 93 percent in the past 8 years. It is unlikely that gonorrhea has declined to a similar extent.

3. The reasons for this difference in response to treatment are not known.

4. Interest in research in gonorrhea is at an all time low in this country.

5. To gain the knowledge needed to press the battle against the gonococcus, there must be a reawakening of interest in gonorrhea among research workers, as well as among those who provide the funds.

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CDC Laboratory Refresher Training Courses

The Communicable Disease Center of the Public Health Service will give its annual laboratory refresher training courses in Chamblee, Ga., July 1956 through June 1957, according to the following schedule:

Laboratory methods in the diagnosis of bacterial diseases:
- Part 1. General bacteriology. September 10–21.
- Part 2. General bacteriology. September 24–October 5.
- Enteric bacteriology. October 8–19.

Laboratory methods in the diagnosis of parasitic diseases:
- Part 1. Intestinal parasites. September 10–October 5.
- Part 2. Blood parasites. October 8–26.

Laboratory methods in the diagnosis of viral and rickettsial diseases. October 15–26.

Laboratory methods in the diagnosis of rabies. October 29–November 2.

Laboratory methods in medical mycology:
- Part 1. Cutaneous pathogenic fungi. January 7–18.
- Part 2. Subcutaneous and systemic fungi. (Completion of part 1 or the equivalent education or experience is a prerequisite.) January 21–February 1.

Laboratory methods in the diagnosis of tuberculosis. January 21–February 1.

Laboratory methods in the study of pulmonary mycoses. February 4–15.

Laboratory diagnostic methods in veterinary mycology. February 25–March 1.

Laboratory methods in the diagnosis of viral and rickettsial diseases. March 11–22.

Serologic methods in the diagnosis of parasitic and mycotic infections. March 11–22.

Laboratory methods in the diagnosis of rabies. March 25–29.

By special arrangement the following courses will be offered:
- Laboratory methods in the diagnosis of malaria.
- Virus isolation and identification techniques.
- Typing of *Corynebacterium diphtheriae*.
- Special problems in enteric bacteriology.
- Phage typing of *Salmonella typhosa*.
- Laboratory methods in diagnosis of leptospirosis.
- Serologic differentiation of streptococci.

Information and application forms should be requested from Laboratory Training Services, Communicable Disease Center, Public Health Service, P. O. Box 185, Chamblee, Ga.

Variation in Mortality From Heart Disease

—*Race, Sex, and Socioeconomic Status*—

By ABRAHAM M. LILIENFELD, M.D., M.P.H.

ONE of the more important reasons for obtaining knowledge of the distribution of a disease in a population is that such knowledge provides a means by which hypotheses concerning pathogenesis can be evaluated. If a hypothesis does not adequately account for at least a majority of the epidemiological features of a disease, it will have to be modified in whole or in part.

The distribution of coronary disease in various socioeconomic groups of the population is particularly pertinent to several etiological hypotheses that have been advanced. From official studies of occupational mortality, Logan has reported the relative mortality risks from coronary disease in England and Wales for five social classes (*1–3*). He has observed that among men the highest social class has consistently had (both in 1930–32 and 1950) the highest mortality from coronary disease and that the mortality risk decreases with a decrease in social status. For married women the social class variation has not been as large nor as consistent. In 1930–32 the pattern for married women was similar to that observed among men, but in 1950 little variation by social class was noted in those aged 20–64. For married women 65 years of age and over the social class pattern of proportionate mortality ratios was similar to that observed among men, although it must be realized that proportionate mortality ratios are difficult to interpret. These distributions may be considered as being consistent with the hypothesis proposed by Keys that excessive fat consumption is an important etiological factor in coronary disease (*4*). It is also consistent with the observation made by Morris and his associates that physical inactivity increases the risk of coronary disease (*5*).

Logan has also reported the results of an analysis of mortality from other forms of myocardial degeneration in England and Wales (*1–3*). The social class distribution for this category is exactly opposite to that observed for mortality from coronary disease; that is, the mortality risk is highest in the lowest social class and it decreases with an increase in social status. This observation suggests that the social class differences with regard to coronary disease mortality might be the result of variation in diagnostic practices in the various social classes. It is conceivable that the greater availability of medical care may have increased the number of diagnoses of coronary disease in the upper income groups.

Dr. Lilienfeld is chief of the department of statistics and epidemiology, Roswell Park Memorial Institute, Buffalo, N. Y., and associate professor of preventive medicine and public health, University of Buffalo Medical School. He began the study reported here while he was assistant professor of epidemiology, Johns Hopkins University School of Hygiene and Public Health. *Dr. Matthew Tayback, chief of the statistical section, Baltimore City Health Department provided the necessary records for the study.*

In view of the difficulties of diagnosis for the various forms of heart disease, it occurred to me that a combination of the deaths from coronary disease and other myocardial degeneration might be about the same for all social groups. In an attempt to study this particular question, I have made an analysis of the mortality from heart disease in Baltimore, Md., for the 3-year period 1949 through 1951. This report presents the results of that analysis. In addition to data on coronary disease and myocardial degeneration, data on hypertension and other forms of heart disease are included.

Method of Study

During the period 1949 through 1951, 14,504 deaths certified as due to heart disease were recorded in Baltimore. Of these, 3,016, or about 21 percent, occurred in the nonwhite population. The distribution of deaths for five categories of heart disease by race and sex are presented in table 1.

To estimate the socioeconomic status for each heart disease death, information concerning characteristics of census tracts in Baltimore published by the United States Bureau of the Census was used. The census tract comprises a neighborhood of between 3,000 and 6,000 persons who are relatively homogenous with regard to such characteristics as median monthly rental, occupational status, and extent of home ownership.

The census tracts in Baltimore were ranked according to the median monthly rental as determined in the 1950 census and then assembled into fifths so that about 20 percent of the city's population of about 950,000 fell into each fifth. The median monthly rental was considered a valid index of relative socioeconomic status because of its high correlation with the other indexes, such as family income, years of school completed, and occupation. The lowest socioeconomic fifth was designated 1; the next fifth, 2; and so on. Each heart disease death was assigned to a socioeconomic fifth on the basis of its allocation to a given census tract from the street address on the death certificate.

One possible limitation to this method of socioeconomic classification, particularly with regard to nonwhite persons, should be noted. Because the method is based on average characteristics of an area rather than actual characteristics of an individual, nonwhites, for example, may be classified in a socioeconomic group higher than their socioeconomic circumstances warrant when they are located in a census tract that is predominantly white. The same difficulty is present with regard to the white population but probably to a lesser extent. However, census-tract classification provides an inexpensive and readily available method for studying the socioeconomic distribution of mortality from a disease.

For comparison with the Baltimore data, some of the data for England and Wales reported by Logan will be presented. In the British reports on social distribution, classification is based on occupational groups. According to the 1951 census, 3.3 percent of the male population aged 15 years and over falls into social class I (professional); 15.0 percent in class II (intermediate between I and III); 52.7 percent in class III (skilled); 16.2 percent in class

Table 1. Number of deaths from various types of heart disease, by race and sex, Baltimore, 1949–51

Type of heart disease [1]	White		Nonwhite		Total
	Male	Female	Male	Female	
Arteriosclerotic heart disease, including coronary disease (420)	3, 296	1, 987	389	236	5, 908
Other myocardial degeneration (422)	1, 194	1, 252	357	308	3, 111
Hypertensive disease with mention of heart disease (440–443)	999	1, 418	542	682	3, 641
Hypertensive disease without mention of heart disease (444–447)	74	84	62	65	285
All other types	592	595	196	176	1, 559
Total	6, 155	5, 336	1, 546	1, 467	14, 504

[1] Numbers in parentheses are category numbers of the International Statistical Classification of Diseases Injuries, and Causes of Death, sixth revision of the International Lists, 1948.

IV (semiskilled); and 12.8 percent in class V (unskilled) (*2*, *3*). Thus, the English social classes I and II are roughly comparable to the Baltimore socioeconomic fifth 5; social class III, to socioeconomic fifths 3 and 4; social class IV, to socioeconomic fifth 2; and social class V, to socioeconomic fifth 1. By presenting this information, I do not intend to imply that the two classifications are completely comparable; it merely gives some idea of their comparability with regard to the percentage of population in each class.

In making comparisons between sexes, races, and socioeconomic groups, differences in the age composition of the population in these groups must be taken into account. This can be done readily by the method of age adjustment commonly employed in routine vital statistics practice. For this study, the standard population used for age adjustment was the total population of Baltimore in 1950. The data presented for each sex, racial, and socioeconomic group are average annual age-adjusted death rates and are therefore directly comparable.

In the British reports, an indirect method of age adjustment resulting in an index termed the standardized mortality ratio was used. Since this method differs from the one used to describe the Baltimore experience, the results cannot be directly compared in absolute terms. However, comparisons can be made between the social classes within each of the two geographic areas, and it is with such comparisons that we are concerned. The interested reader is referred to the text on medical statistics by Bradford Hill, where these methods of age adjustment are discussed (*6*).

Arteriosclerotic Heart Disease

The International List category designated arteriosclerotic heart disease includes three subcategories: arteriosclerotic heart disease, coronary artery disease, and angina pectoris. All heart disease deaths in which coronary artery disease is mentioned are placed in this category, but, admittedly, deaths not due to coronary disease are also included. This category was used as representing deaths from coronary disease in the analysis of mortality in England and Wales in 1949 and 1950. It would appear reasonable to assume that if there are significant racial, sex, or socioeconomic variations in mortality from coronary disease, it would be possible to detect them by an analysis of this category of deaths, unless, of course, the distributions of each subcategory are in opposite directions.

Table 2. Average annual age-adjusted death rates per 10,000 population for arteriosclerotic heart disease (including coronary disease)[1] by race, sex, and socioeconomic status, Baltimore, 1949–51

Socioeconomic fifth	White		Nonwhite	
	Male	Female	Male	Female
1 (lowest)	29. 2	15. 9	20. 7	11. 4
2	34. 6	14. 7	14. 4	7. 4
3	33. 0	12. 1	15. 2	9. 6
4	29. 9	14. 0	[2] 17. 5	[2] 14. 8
5 (highest	32. 3	13. 0	[2] 24. 8	[2] 9. 0

[1] International List No. 420.
[2] Based on population of less than 1,000.

The results of the analysis of mortality from arteriosclerotic heart disease in Baltimore are presented in table 2. It is to be noted that males have markedly higher death rates than females, in both racial groups and in all socioeconomic groups. But perhaps of more interest is the fact that there is no particular pattern of variation in mortality for the different socioeconomic groups; the differences between socioeconomic groups may well be due to chance variation.

The lack of a socioeconomic pattern in Baltimore is in marked contrast to the findings on

Table 3. Standardized mortality ratios for deaths from coronary heart disease for males and married females aged 20–64 years, by social class, England and Wales, 1950[1]

Social class	Male	Married females
I—Professional	150	92
II—Intermediate between I and III	110	93
III—Skilled workers	104	101
IV—Semiskilled workers	79	100
V—Unskilled workers	89	108

[1] From reference 2.

social class distribution in England and Wales in 1950, which are shown in table 3. In England and Wales, there is an increasing gradient of mortality ratios from the lowest class to the highest among men, and there is a slightly increasing gradient in the reverse direction among married women. Admittedly, the Baltimore and the English data are not strictly comparable. The methods of classifying socioeconomic status differ, and the English data are limited to age groups 20–64 years. (The data for persons aged 65 and over are not presented here because they are expressed as proportionate mortality ratios.) Also, there are differences in the reporting and classification of causes of death: For example, in England the term "arteriosclerotic heart disease" is infrequently used in reporting causes of death. Nonetheless, it seems reasonable to expect that if social class variations in mortality from coronary disease did exist in Baltimore as they appear to exist in England, they should have been evident in the data presented in this report.

Table 4. Average annual age-adjusted death rates per 10,000 population for other myocardial degeneration,[1] by race, sex, and socioeconomic status, Baltimore, 1949–51

Socioeconomic fifth	White		Nonwhite	
	Male	Female	Male	Female
1 (lowest)	20. 1	12. 8	22. 5	16. 9
2	13. 5	10. 9	13. 3	14. 2
3	12. 7	9. 4	13. 7	12. 1
4	9. 3	7. 2	[2] 11. 7	[2] 11. 4
5 (highest)	8. 4	7. 1	[2] 6. 2	[2] 4. 3

[1] International List No. 422.
[2] Based on population of less than 1,000.

Table 5. Standardized mortality ratios for deaths from myocardial degeneration for males and married females aged 20-64 years, by social class, England and Wales, 1950[1]

Social class	Male	Married females
I—Professional	67	66
II—Intermediate between I and III	82	67
III—Skilled workers	97	98
IV—Semiskilled workers	98	120
V—Unskilled workers	137	134

[1] From reference 2.

Table 6. Average annual age-adjusted death rates per 10,000 population for hypertension with and without mention of heart disease, by race, sex, and socioeconomic status, Baltimore, 1949–51

Socioeconomic fifth	White		Nonwhite	
	Male	Female	Male	Female
	With mention of heart disease[1]			
1 (lowest)	12. 1	13. 9	27. 6	33. 5
2	9. 9	12. 6	21. 8	25. 8
3	11. 8	12. 0	23. 9	24. 6
4	7. 7	9. 9	[3] 19. 1	[3] 17. 7
5 (highest)	9. 0	7. 7	[3] 22. 0	[3] 21. 6
	Without mention of heart disease[2]			
1 (lowest)	0. 7	0. 6	1. 9	3. 3
2	. 8	. 9	1. 7	1. 8
3	. 8	. 7	2. 9	2. 2
4	. 7	. 6	[3] 3. 0	[3] 1. 3
5 (highest)	. 7	. 5	[3] 0	[3] 0

[1] International List Nos. 440–443.
[2] International List Nos. 444–447.
[3] Based on population of less than 1,000.

Myocardial Degeneration

The age-adjusted rates for deaths from other myocardial degeneration in Baltimore are presented in table 4. This category, according to the International List, includes such terms as fatty degeneration, myocardial degeneration with arteriosclerosis, cardiovascular degeneration, atheroma of heart or myocardium, and chronic myocarditis.

In general, the rates for white males are higher than the rates for white females, but there is little difference between the sexes for the nonwhite population. In addition, the white and nonwhite male rates are nearly the same. Thus, the nonwhite rates for both sexes are similar to the white male rates, and the white female rates are lower than the rates for the other three groups. This general pattern, which is present for all the socioeconomic groups, differs from that observed for deaths due to arteriosclerotic heart disease. The socio-

economic distribution also differs from that for arteriosclerotic heart disease. There is a decreasing gradient of mortality from the lowest socioeconomic group to the highest, for both races and both sexes.

The social distribution of mortality from myocardial degeneration in England and Wales in 1950 in shown in table 5. For this category of heart disease, the pattern is similar to that for Baltimore. This similarity perhaps increases the significance of the lack of consistency between the two areas with regard to coronary heart disease deaths. It would not seem that differences in the method of classification of social classes or the limitation to a certain age group would produce differences in the patterns of one group of deaths and not in the patterns of another.

Hypertensive Disease

Classified in the International List under hypertensive disease are eight categories. For this report, these have been grouped into (*a*) hypertension with mention of heart disease and (*b*) hypertension without mention of heart disease. The rates for these two groups are presented in table 6. Since there are only a few deaths classified in the second group, no conclusions can be drawn from the data.

For hypertensive disease with mention of heart disease, the rates for the nonwhites are about twice as high as the rates for the whites. This is true for both sexes and for all socioeconomic groups. The rates for the females are higher than the rates for the males in both racial groups. The higher white female rates are present in all socioeconomic groups except the highest group, where the male rate exceeds the female rate. Among the nonwhites, the female rate is higher than the male rate in the three lower socioeconomic groups, but a suggested reversal occurs in the two upper socioeconomic groups. This change in mortality relative to sex and social class, which occurs in both races, may be of some epidemiological interest and worthy of further investigation.

Table 7. Average annual age-specific death rates per 10,000 population for arteriosclerotic heart disease (including coronary disease),[1] by race, sex, and socioeconomic status, Baltimore, 1949–51

Age group (years)	Male					Female				
	Socioeconomic fifth					Socioeconomic fifth				
	1 (lowest)	2	3	4	5 (highest)	1 (lowest)	2	3	4	5 (highest)
	White									
Under 25	0	0	0	0	0	0	0	0	0	0
25–34	1.0	.8	1.6	.7	.2	.3	.4	.3	0	0
35–44	10.5	13.4	7.6	9.6	9.2	1.3	1.0	1.1	.7	.4
45–54	51.2	38.9	39.7	43.9	36.8	9.7	8.9	7.8	6.4	5.5
55–64	101.9	100.2	112.1	109.7	93.5	42.8	41.4	34.2	27.2	27.0
65–74	151.7	212.8	183.8	114.2	203.5	108.5	85.8	102.2	69.2	100.2
75 and over	190.1	354.6	334.5	332.0	346.9	233.0	243.1	120.7	268.7	219.7
	Nonwhite									
Under 25	2.0	0	0	0	[2] 0	0	0	0	0	[2] 0
25–34	0	0	7.6	[2] 13.1	[2] 0	0	2.6	1.6	[2] 0	[2] 0
35–44	32.3	9.3	16.8	[2] 0	[2] 131.6	10.0	1.5	11.9	[2] 0	[2] 0
45–54	60.4	75.1	71.4	[2] 14.4	[2] 59.5	46.2	35.1	39.0	[2] 47.5	[2] 0
55–64	240.3	169.0	134.8	[2] 105.0	[2] 161.3	136.4	98.0	94.6	[2] 146.3	[2] 155.0
65–74	[2] 335.8	244.1	[2] 293.0	[2] 352.9	[2] 0	[2] 199.6	97.3	146.6	[2] 289.9	[2] 259.7
75 and over	[2] 471.0	[2] 219.2	[2] 260.2	[2] 980.4	[2] 1,500.0	[2] 213.3	[2] 161.3	[2] 282.4	[2] 483.9	[2] 0

[1] International List No. 420.

[2] Based on population of less than 1,000.

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It seems that the lower socioeconomic groups have a higher mortality from hypertensive disease (with mention of heart disease) than the upper groups, and, among females of both races, there is a suggestion of a decreasing gradient from the lowest socioeconomic group to the highest. This pattern can be considered as suggestive only, particularly since it is not clearcut for the males of either race.

Other Results

In view of the differences between the Baltimore and the English experiences with regard to coronary disease deaths, I thought that perhaps the method of age adjustment might be concealing existing differences between social classes. For a better comparison of the mortality in the various social groups, age-specific death rates for three categories of heart disease are presented in tables 7 through 9. Examination of these rates confirms the existence of the patterns noted in the analysis of the age-adjusted rates.

The deaths classified in the remaining heart disease categories in the International List were grouped together, and the age-adjusted rates are presented in table 10. Owing to the heterogeneity of this group, no inferences can be drawn. Unfortunately, no one form of heart disease in this group could be singled out for further study because of the small number of deaths.

Discussion

Before discussing the inferences that can be derived from the results of this analysis, attention should be directed to some of the limitations of the data. Of prime importance is the question of the accuracy of cause-of-death statements on death certificates. Recently, James, Patton, and Heslin reported an "appreciable degree" of inaccuracy when the causes of death on death certificates were compared with autopsy findings (*7*). The possibility of inaccuracy in cause-of-death statements imposes a serious limitation on what can be inferred from

Table 8. Average annual age-specific death rates per 10,000 population for other myocardial degeneration,[1] by race, sex, and socioeconomic status, Baltimore, 1949–51

Age group (years)	Male					Female				
	Socioeconomic fifth					Socioeconomic fifth				
	1 (lowest)	2	3	4	5 (highest)	1 (lowest)	2	3	4	5 (highest)
	White									
Under 25	0	0	0	0	0	0	0	0	0	0
25–34	0	0	.3	0	0	0	0	0	0	0
35–44	.8	.5	1.4	.5	.2	.4	.5	.4	.5	.6
45–54	10.9	2.9	8.4	1.4	2.4	4.0	2.4	2.5	1.6	1.2
55–64	41.0	31.0	19.4	17.2	8.9	23.1	11.5	11.8	5.1	5.1
65–74	125.4	77.4	77.4	43.3	52.5	56.4	52.5	42.4	34.2	31.0
75 and over	395.6	297.0	264.2	247.1	214.9	337.8	315.7	268.5	220.4	222.4
	Nonwhite									
Under 25	0	1.7	2.7	0	[2] 0	0	1.4	0	0	[2] 0
25–34	0	1.4	0	[2] 13.1	[2] 0	1.4	0	0	[2] 0	[2] 0
35–44	10.2	6.2	6.3	[2] 0	[2] 0	14.9	10.5	4.0	[2] 0	[2] 0
45–54	78.2	48.0	62.5	[2] 57.6	[2] 0	41.1	17.5	47.9	[2] 15.8	[2] 0
55–64	240.3	88.5	99.7	[2] 105.0	[2] 0	160.0	119.2	133.6	[2] 122.0	[2] 0
65–74	[2] 451.2	286.2	[2] 293.0	[2] 235.3	363.6	[2] 354.8	215.4	199.6	[2] 144.9	[2] 129.9
75 and over	[2] 797.1	[2] 438.4	[2] 334.6	[2] 196.0	[2] 0	[2] 453.3	[2] 383.1	[2] 352.9	[2] 645.2	[2] 294.1

[1] International List No. 422. [2] Based on population of less than 1,000.

Table 9. Average annual age-specific death rates per 10,000 population for hypertension with mention of heart disease,[1] by race, sex, and socioeconomic status, Baltimore, 1949–51

Age group (years)	Male					Female				
	Socioeconomic fifth					Socioeconomic fifth				
	1 (lowest)	2	3	4	5 (highest)	1 (lowest)	2	3	4	5 (highest)
	White									
Under 25	0.1	0	0	0.1	0	0	0	0	0	0
25–34	.3	.4	0	.2	0	0	.3	0	.3	0
35–44	1.6	1.9	1.4	1.2	.9	2.6	4.3	.4	1.4	.6
45–54	9.4	7.4	9.3	7.8	6.2	15.4	10.1	10.2	7.4	4.5
55–64	31.1	32.6	25.7	19.2	22.2	31.6	26.1	34.8	23.1	15.6
65–74	87.2	62.9	73.1	39.8	61.4	79.2	79.4	66.6	59.7	47.0
75 and over	156.4	115.2	188.3	127.4	135.7	220.0	191.8	191.0	167.5	149.2
	Nonwhite									
Under 25	0	0	2.7	0	[2] 0	0	0	0	0	[2] 0
25–34	8.0	5.5	0	[2] 0	[2] 0	5.5	5.1	8.1	[2] 11.3	[2] 0
35–44	35.7	21.8	14.7	[2] 81.7	[2] 0	51.4	49.4	33.6	[2] 25.5	[2] 52.4
45–54	120.7	68.9	89.3	[2] 57.6	[2] 0	171.9	135.9	125.8	[2] 47.5	[2] 42.4
55–64	299.2	257.6	193.4	[2] 210.0	[2] 80.7	326.2	289.5	239.3	[2] 219.5	[2] 0
65–74	[2] 346.3	370.4	[2] 512.8	[2] 117.7	[2] 727.3	[2] 510.0	354.4	389.7	[2] 289.9	[2] 259.7
75 and over	[2] 760.9	[2] 493.2	[2] 632.0	[2] 588.2	[2] 1,000.0	[2] 693.3	[2] 362.9	[2] 470.6	[2] 322.6	[2] 1,764.7

[1] International List Nos. 440–443. [2] Based on population of less than 1,000.

the analysis of mortality data. But analysis of death certificate information is a readily available, inexpensive means of studying distributions of certain diseases, and it is generally considered a satisfactory method of uncovering areas for further investigation. Another limitation, as already pointed out, results from the use of census tracts as a means of socioeconomic classification.

The initial interest in this analysis was to determine whether the social pattern of coronary disease mortality observed in England and Wales might be due to differences in diagnostic practices in the various social classes. It seemed that this might be inferred if a similar pattern were observed in Baltimore and if a combination of the deaths from coronary disease and other myocardial degeneration should result in a disappearance of the social differential. But the distribution of coronary disease deaths was not found to be like the English pattern. If the two categories were combined, the highest socioeconomic fifth would have the lowest rates, and there would be an increase in the mortality risk with a decrease in socioeconomic status. On the other hand, a reviewer of this paper has shown that when the English data for these two categories are combined, the highest social class still has the highest rates, although the difference between social classes is diminished.

Table 10. Average annual age-adjusted death rates per 10,000 population for all other forms of heart disease, by race, sex, and socioeconomic status, Baltimore, 1949–51

Socioeconomic fifth	White		Nonwhite	
	Male	Female	Male	Female
1 (lowest)	7.0	5.5	14.3	7.2
2	6.7	5.5	12.3	6.7
3	6.3	4.2	13.8	6.6
4	4.6	3.8	[1] 15.6	[1] 4.8
5 (highest)	4.9	4.0	[1] 8.5	[1] 12.7

[1] Based on population of less than 1,000.

To explain the discrepancies between the Baltimore and English experiences, one is tempted to postulate the existence of possible biological differences. For example, from the viewpoint of a dietary hypothesis of coronary heart disease, it is conceivable that there may be differences in dietary habits among the social classes in England that do not exist in Baltimore. But before hypothesizing this type of explanation, it would be necessary to eliminate the possible influence of nonbiological differences, such as methods of social classification and of death certification and diagnostic practices.

The present analysis also raises the question as to whether the pattern observed in England and Wales can be used as a test of the consistency of any particular etiological hypothesis of coronary disease with the social distribution of mortality from this disease. If the social distributions were found to be similar in many geographic areas, the confidence with which these distributions could be used as an index of the validity of an etiological hypothesis would be increased. The apparent existence of dissimilar distributions in Baltimore and in England and Wales suggests the need for further investigation of social variations in heart disease mortality.

Summary

From information on certified deaths in Baltimore during the period 1949 through 1951, mortality from various types of heart disease was analyzed by race, sex, and socioeconomic status.

Mortality rates for arteriosclerotic heart disease (including coronary artery disease) were observed to be higher among males than among females and higher in the white population than in the nonwhite. No significant differences were noted in the rates for five socioeconomic groups. This latter observation is in contrast to the social distribution found in England and Wales, where the risk of dying from coronary disease is highest in the upper social classes.

Mortality rates for myocardial degeneration were higher among white males than among white females. Among the nonwhites, no essential differences were noted between the sexes. The rates for the nonwhites were somewhat higher than those for the whites. For both sexes and both races, the highest rates were noted in the lowest socioeconomic group, with a gradual decrease in rates with an increase in socioeconomic status. This social distribution is similar to that observed in England and Wales.

Mortality rates for hypertensive disease were higher in the nonwhite population than in the white. The lowest socioeconomic group had the highest rates, and there tended to be a decrease in rates with an increase in socioeconomic status, although the pattern was not regular. The female rates were higher than the male rates in the lower socioeconomic groups, whereas the reverse was true in the upper groups; this was observed for both races.

The use of death certificate information for analysis of mortality and the use of census tracts for socioeconomic classification both impose certain limitations on the data derived. Nonetheless, the apparent existence of differences in the social distribution of coronary disease deaths in two geographic areas indicates a need for further study of the subject.

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The epidemiology of the septic tank is described with suggestions for helping builders of mass housing to prevent future disease outbreaks and nuisances.

Sewage Disposal in Mass Building

By DAVID B. LEE, M.S. in Eng.

IN the past 10 years, the urban fringe has seen the installation of millions of septic tanks, far more than had been eliminated by sanitary engineering services in the previous 50 years.

The septic tank has been installed not only for those who have land and income generous enough to accommodate and maintain the facility, but for families who have neither the space nor the resources to prevent the development of a sanitary nuisance and a public health hazard. Often such families must go to the expense of a new installation or, if possible, thorough reconstruction. Septic tanks may work well in rural areas if people do not live too close to each other or use a great deal of water for bathing, laundry, air conditioning, and dishwashing.

To put it simply, a septic tank is a country cousin that came to town and promptly got into trouble. In its place—a rural setting—the septic tank and subsurface drain field is a suitable method of domestic sewage disposal, given adequate drainage, soil conditions, and water table; but it was never intended for use in settlements with more than one family dwelling per acre. Even this may be too dense for septic tanks if soil conditions and water tables are not ideal.

Where public facilities cannot be arranged, the septic tank soil absorption system of sewage disposal, originally designed for rural areas, is now widely utilized as a convenient and temporary substitute. Under rural conditions and with proper design, construction, and maintenance, this system will usually give some degree of satisfactory performance.

If failure of the soil absorption system occurs under rural conditions, the danger to public health is minimum since there are plentiful opportunities to choose another location for a new system. In urban areas, the septic tank is often a needless and frequently an extravagant method of sewage disposal which threatens to be a sanitary nuisance and a public health hazard to millions of homeowners.

Then, why have there been so many septic tanks installed during the past 10 years?

The following discussion will attempt to explain why builders adopt these expedient but short-sighted construction methods and to suggest what may be done about it.

The epidemiology of the septic tank itself suggests therapeutic and preventive measures for this form of community sickness, a sickness that is appraised not only by the number of individual infections but by nuisance, expense, and disorder. It is the business of public health to treat the community as the physician treats the person. And in view of the prospect of the continuing building boom, it is the business of public health to assure that this community sickness will not prevent or stunt healthy community growth.

Mr. Lee is director of the bureau of sanitary engineering, Florida State Board of Health, Jacksonville, Fla.

Builders Are Human

In my judgment, the postwar building program is yet to reach its peak in many areas of the country. The housing deficit, accumulated since 1926, has been overcome only in isolated communities and for isolated income groups. Much of the housing built since 1940 has been only a temporary palliative to housing needs. Millions of units, fundamentally well-built and well-equipped, are already too small for growing families. With rising incomes, families are demanding more of housing. If you add to these factors the steady obsolescence of aging buildings, spatial shifts of population, and the rising birth rate, it is apparent that the current production rate of 1.3 million dwelling units a year is not excessive.

Accurate figures are not available, but in my opinion the estimate that at least 24 million persons in the United States are served by 6 million individual septic tank systems is close to the truth. More important, however, is the estimate that more than one-third of the new homes now being constructed will have septic tank systems for sewage disposal. All of this continues against the better judgment of many in the public health profession, and presents one of the greatest challenges sanitary engineers and other public health workers will have to face in the years to come. Must we abet septic tanks?

The mass building industry is chronically in need of land, low-priced land, in large tracts. Such land is seldom to be found within city limits, where zoning laws and city plans apply, and where community water and sewerage facilities are likely to be present or required.

Mass builders usually find the land they need in territory where inhabitants or governing authorities have had meager or limited experience in urban development. It is unlikely that in such an area there is any local person equipped to supervise the builders and their sewage disposal plans. The burden of supervision usually falls on the county and State officials and, in some instances, on the insuring and lending agencies. Even so, in the interest of profit and sound construction, progressive mass builders would prefer to put in community water and

Serving several subdivisions, this activated sludge plant houses two primary mechanical aerator units, a sludge digester, laboratory, pump room, office, and truck loading room for digested sludge. The slump brick terrace (lower terrace) is a chlorine contact chamber and the higher terrace (second floor level) is a secondary clarifier.

sewerage facilities. What stands between them and their better judgment is a matter of money.

Typically, a builder does not construct 200 houses wholesale and then sell them in one lot. In phase building, he finishes one house at a time. And he sells one at a time, as the units are finished. Even if his sales are committed in advance, settlement of the title is closed only as the individual houses are finished.

Naturally, he wishes to recover water and sewerage installation costs on each house as it is sold. Such recovery is easiest when the house has a private well and septic tank.

It is not as easy to recapture the investment in community facilities with any rapidity. To provide community sewerage facilities for no more than 500 units would tie up between $150,000 and $200,000 while the houses are in construction. It may take a little time before this investment can be freed. There have been few, if any, financial institutions willing to carry that kind of investment, especially for builders who may sell no more than 50 to 100 houses a year. Such financing is certainly not practical for the typical builder who needs a fast turnover on limited capital simply to keep himself going. Even mass builders are susceptible to the appeal of the fast return of their

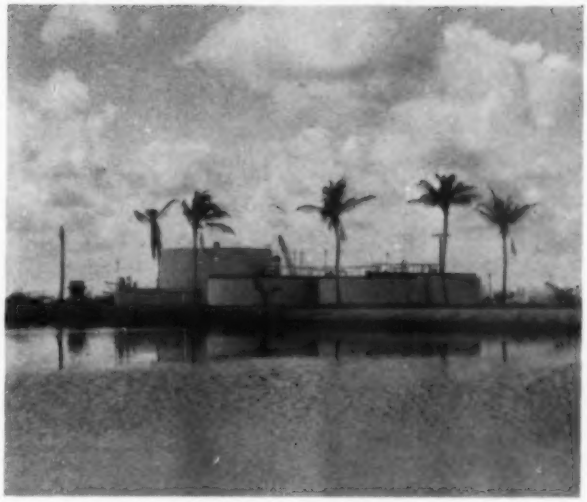
money. Some have ventured to use septic tanks with projects of as many as 8,000 homes and larger.

The Cost of Services

Given financing, it would be to the great advantage of both the builder and the community to install community water and sewerage facilities. To deal with sewage disposal alone, the Florida builder can install sewers at a charge ranging from $150 to $250 per lot. To include the cost of sewage treatment facilities for 500 families in my own State would run the total charge for sewage disposal facilities to from $300 to $400 a dwelling.

The superior attraction of a house with sewerage connections will enhance the market value of the structure by some amount over and above the ordinary charge for septic tank installations. Although the increased value of the house may return a price that will pay for the community sewage collection and treatment facilities, title to the plant would remain with the builder. Furthermore, by collecting sewage service charges, he may cover operating, maintenance, and amortization costs, and so recover his investment. Meanwhile, the community would have the advantage of a trouble-free waste disposal system. The gross income from 500 houses with community water supply and community sewerage may amount to approximately $30,000 a year. Such an operation is practical with as few as 200 houses.

Aeration tank and public water supply tank in the background with the sludge digester and control house in the foreground serving Carol City, Fla., near Miami.



Carol City activated sludge plant as seen from across the manmade lake into which the effluent discharges.

Recognizing such financial advantages, 120 subdivisions in Florida have installed their own community sewage disposal facilities and community water systems in the past 5 years. But several were motivated also by a stern refusal by government officials to permit septic tank construction in areas where such disposal methods are no longer suitable.

It can often be demonstrated that the average cost of a septic tank and subsurface disposal system and the cost of maintaining and operating such a system are certainly equal to, and, in many cases, more expensive than a monthly sewer service charge for a method of sewage disposal that is not only safe but trouble free.

Corrective Measures

Once septic tanks are in, especially in areas with a high water table, poor soil conditions, and relatively dense settlement, the corrective measures frequently require that they be bypassed. They may serve well during dry periods but let the rains come and in no time the soil is saturated: From the ground surface noxious gases will come forth; septic tank effluents will appear on the ground; they may

back up into bath tubs or prevent the flushing of commodes.

As this was written, on January 24, 1956, two ladies called me to report that more than 100 septic tanks in their subdivision had failed in the past 24 hours. The gases coming back through the plumbing and into the house were so serious that the house had to be opened and the attic fan used to freshen the air. This was besides the fact that the yard was flooded with septic tank effluent.

In one subdivision with 180 homes of a high financial bracket, soil conditions were such during 1955 that 25 homeowners were obliged to construct relief sewers from their drain field to the roadside ditch in order to allow the wastes to escape.

Since sewerage is the only practical correction for defective septic tank installation, it seems obvious that in mass building projects sewers should be installed when the homes are built.

We, in Florida, recommend that plumbing in all new houses be so constructed and septic tanks, when used, be so located—on the side of the house or in the front—as to facilitate eventual connection to a sanitary sewer.

Preventive Measures

What can be done to assure that mass housing projects of the future will be built with adequate community sewerage facilities?

Of all possible means of preventing undesirable septic tank construction in the future, aggressive, direct efforts by government officials, by builders, and by insuring and financing agencies are most likely to produce results. Governments and political subdivisions can strive to overcome artificial political barriers which today strangle rational urban growth, and which, in fact, encourage undesirable building in outlying areas at the expense of well-established urban centers. Whether it is done by creating sanitary districts, metropolitan or regional planning authorities, county and State zoning officials, new boundaries, or local government holding companies, the accommodation of urban growth is a primary political responsibility of local and State governments.

If local and State governments impart such political muscle to zoning and planning commissions, it cannot be too heavily stressed that members of such commissions should be independent of financial pressure and political and special interests. Commissions should be staffed by qualified and intelligent laymen as well as professional personnel with merit system status. They should also be sensitive to the welfare of the people and be interested only in the development of the area they serve and the part it plays in the development of the State and the Nation.

The most immediate opportunity for good work in urban growth, however, is in the hands of agencies which insure, guarantee, or underwrite funds for residential construction and development. It would be to their own interest and protection to assure loans for community water and sewerage facilities and to require such systems for all dwellers whose financing they insure in mass building developments. If these agencies would do no more than agree to insure mortgages on community facilities, builders, the financial people, sanitary engineers, and others will certainly work out the details. In my opinion, the greatest need in housing today is for leadership in the financing of community water and sewerage facilities.

Summing Up

Based on my experience, it has been demonstrated that the septic tank in congested neighborhoods is uneconomic, unwise, and unwholesome. Its widespread use in recent years may be due largely to the failure of local government officials to assure wise and orderly development of new neighborhoods and to the failure of financial institutions to encourage builders to install community sewerage facilities. Since sewerage facilities are the only practical alternative to the use of septic tanks, their construction must be encouraged if we are to avert the installation of millions of septic tanks in the next 10 years. All government agencies need to organize better methods of managing urban and suburban growth. But immediate benefits will result from agreements by insuring and lending agencies to finance community facilities for water supply and sewage collection and treatment.

50 years — of Food and Drug Protection

By GEORGE P. LARRICK
Commissioner of Food and Drugs

This section of *Public Health Reports* is devoted to an account of some of the principal programs of the Food and Drug Administration which affect public health.

It is an appropriate way to commemorate the golden anniversary of our first Federal pure food and drug law, not so much by reviewing the past as by considering the challenge of the future.

The articles are by men directly concerned with the administration of the programs. It is notable that they consistently emphasize technological changes in foods, drugs, and cosmetics, affecting an important part of the human environment.

From the beginning the food and drug law has been directed at specific abuses: errors of omission or commission which can be proved in a court of law. Likewise, the law has from its beginning reflected the standard of achievement attained by the majority of producers of foods and drugs and has required the backward element to meet that same standard.

As a result, food and drug law enforcement has been a stimulus to industrial progress as well as a direct and practical means for dealing with important environmental health hazards.

The original Pure Food and Drugs Act which Theodore Roosevelt signed into law on June 30, 1906, was one of the great milestones of public health progress. Few, if any, events have had a greater effect in promoting such objectives as the sanitary handling of food or rational therapeutics in medicine. It would be fitting to dedicate these papers to Dr. Harvey W. Wiley, who, more than any other, was responsible for the enactment of this law.

Each generation needs to learn anew the why and wherefore of its institutions and blessings; otherwise they are taken for granted. Today, the right of the public to pure foods, effective drugs, safe cosmetics, and truthful labels has become generally accepted. It was not always so. We need to be reminded of Dr. Wiley and his 23-year struggle to obtain our first Federal pure food and drug law. It helps us understand and appreciate the value of the protective laws we now have, and the truly wonderful progress made by our food, drug, and cosmetic industries in this half century. It also helps us understand our problems of today and our obligation to insure that food and drug products of today and tomorrow will continue to be the best in the world.

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Significant Dates in Food and Drug Law History

Since the beginning of recorded history, men who have organized themselves into civilized societies have been concerned about the purity of the food and drink offered to the public.

In 1202, King John of England proclaimed the first English food law, the Assize of Bread. This prohibited adulteration of bread with such ingredients as ground peas or beans.

The history of food and drug measures as it has developed in the United States is set forth in the following chronology:

1784. Enactment by Massachusetts of the first general food law in the United States.

1824. Flour Inspection Act for Alexandria, then in the District of Columbia.

1844. Dr. Harvey Washington Wiley was born October 18 at Kent, Ind.

1848. Edwards law passed to prohibit the importation of adulterated drugs.

1850. A pure food and drink law was passed in California, one year after the gold rush.

1879–1906. During these 27 years more than 100 food and drug acts were introduced in Congress.

1879. Chief Chemist Peter Collier, Division of Chemistry, Department of Agriculture, began a food and drug adulteration investigation.

1880. Peter Collier recommended enactment of a national food and drug law.

1883. Dr. Wiley became chief chemist of the Division of Chemistry of the Department of Agriculture on April 9. Immediately he assigned some members of his staff to study the problems of food and drug adulteration.

1883. The Tea Importation Act was passed, providing for inspection of all tea entering United States ports.

1890. Acts were passed prohibiting importation of adulterated food and drugs and providing for certification of certain exported meat products.

1891–1895. Partial protection of domestic consumers was effected by acts requiring inspection of animals for diseases before slaughtering.

1902. Sherman Act, passed by Congress on July 1, prohibited the false branding of food and dairy products. In this same year appropriations were made by Congress to establish pure food standards.

1906. The first Federal Food and Drugs Act (34 stat. 768), the Heyburn Act, passed Congress and was signed June 30 by President Theodore Roosevelt. The President also signed the Meat Inspection Act on that day.

1907, January 1. The Bureau of Chemistry of the Department of Agriculture, headed by Dr. Wiley, began administration of the Food and Drugs Act of 1906.

1912, March–December. Dr. Wiley was succeeded by Dr. Carl L. Alsberg as chief chemist of the Department of Agriculture. Regulatory and research functions were separated.

1913, March 3. Gould amendment (37 stat. 732), requiring that quantity information on food packages be correct, passed.

1919, July 24. Kenyon amendment (41 stat. 271) passed. It applied net-weight labeling to wrapped meats.

1921, July. Dr. Alsberg was succeeded by Walter G. Campbell, who became acting chief of the Bureau of Chemistry.

1924, July. Mr. Campbell took over all regulatory work of the Bureau of Chemistry as a separate function, as Dr. Charles A. Browne became chief of the Bureau.

1927. A separate law-enforcement agency was formed, first known as the Food, Drug, and Insecticide Administration; then, in 1931, as the Food and Drug Administration. Mr. Campbell became Commissioner of Food and Drugs.

1930. The canning industry supported the McNary-Mapes amendment, authorizing standards of quality and fill of container for canned foods.

1938. The Copeland bill was passed by Congress. It was known as the Food, Drug, and Cosmetic Act of 1938, and contained these new provisions, among others:

- Extended coverage to cosmetics and devices.
- Required predistribution clearance of safety on new drugs.
- Prohibited addition of poisonous or deleterious substances to foods, except where required or unavoidable.
- Provided for tolerances for unavoidable or required poisonous substances.
- Authorized standards of identity, quality, and fill of container for foods.
- Authorized factory inspections.
- Added the remedy of court injunction to previous remedies of seizure and prosecution.

1940, July 1. FDA transferred from the Department of Agriculture to the Federal Security Agency.

1944, May 1. Dr. Paul B. Dunbar succeeded Mr. Campbell as Commissioner of Food and Drugs.

1945, July 6. Federal act amended to require certification of the safety and efficacy of penicillin. Later amendments extended this requirement to other antibiotics.

1948, June 24. Miller amendment (62 stat. 582) affirmed United States jurisdiction over products adulterated or misbranded after interstate shipment.

1951, June 1. Charles W. Crawford succeeded Dr. Dunbar as Commissioner.

1951, October 26. Durham-Humphrey amendment (65 stat. 648) specifically required that drugs which cannot be safely used without medical supervision bear the prescription legend on the label and be dispensed only upon prescription.

1953, August 7. Factory inspection amendment (67 stat. 476) clarified previous provision regarding mandatory factory inspection, and required the issuing to manufacturers of written reports on inspections and analysis of factory samples.

1954, April 15. Hale amendment (68 stat. 54) simplified method of promulgating food standards where no controversy was involved.

1954, August 12. George P. Larrick succeeded Mr. Crawford, who retired as Commissioner.

1955. Secretary Oveta Culp Hobby of the Department of Health, Education, and Welfare appointed a committte of 14 distinguished citizens to study the adequacy of the Food and Drug Administration's facilities and programs.

1955. The Citizens Advisory Committee reported on June 30, recommending a substantial expansion of FDA's facilities, a new building for FDA, and more use of educational and informational programs by FDA.

1956. The 50th anniversary year, a year of tribute and rededication on the part of government and industry to the cause of effective food and drug protection.

THE BIRTHDAY SEAL

Adopted by the Association of Food and Drug Officials

Food Sanitation

By GLENN G. SLOCUM, Ph.D.

In the first annual report of the Bureau of Chemistry, Department of Agriculture, after the passage of the Food and Drugs Act of 1906 (*1*), Dr. Harvey W. Wiley stated: "Any unfavorable conditions found in the factories inspected were subsequently discussed with the inspectors, with a view . . . of impressing upon them the necessity of sanitation in the preparation of articles of food and drugs . . . ." Thus, food sanitation programs were initiated at the inception of enforcement of the first Federal food and drug law. They have continued for 50 years to occupy a prominent position in the work of the Food and Drug Administration.

The Food, Drug, and Cosmetic Act of 1938, like the act of 1906, is basically a statute to protect the public health. Proper sanitation in the production and handling of foods and drugs is one of its major requirements.

A sanitary food, strictly speaking, is one free from injurious substances, particularly infectious micro-organisms. But modern concepts of food control have expanded this definition to include freedom from materials that are repulsive or obnoxious regardless of their importance as agents of disease. This development is an important factor in the protection of health, since many forms of food contamination carry potential health hazards that cannot be measured, even with modern analytical techniques, by objective examination of food products. The expanded definition has become generally accepted by the food industries and the public, and it is firmly established by many court decisions in actions brought under the food and drug laws.

The requirements of the law and the objectives of the Food and Drug Administration with respect to food sanitation may be stated simply: that foods be prepared from clean, sound, and wholesome raw materials and that sanitary conditions prevail at all stages of production and distribution. It has been the consistent policy of the Food and Drug Administration through 50 years of enforcement of the food and drug laws to seek to improve the sanitary quality of the food supply by all means and facilities at its disposal.

Dr. Slocum is chief of the Division of Microbiology, Food and Drug Administration.

The Early Activities

When the Food and Drugs Act was enacted in 1906, interstate traffic in foods was limited primarily to a few staple products. Food production and distribution were largely local operations, and the housewife usually processed the basic raw materials in her home. Although Dr. Wiley and others supporting the drive for legislation were preoccupied with such problems as the use of harmful or potentially harmful chemicals in foods and widespread economic adulteration, writings of that period show that there was a real recognition of and concern with problems of food sanitation.

Early administrative reports of the Bureau of Chemistry, Department of Agriculture—the agency charged with enforcement of the Food

and Drugs Act until the Food and Drug Administration was created in 1927—clearly trace the development of food sanitation programs (*1*). Sanitary requirements of the law were stressed in inspection of all food processing and distributing facilities. Field and laboratory investigations of sanitation were soon initiated for many important commodities, including milk, cream, ice cream, bottled mineral waters, shellfish, gelatin, poultry, and fresh, frozen, and dried eggs. Bacteriological and microscopic methods of analysis for detection of contamination and spoilage were developed and put into use. Research operations not only revealed enforcement problems and methods for the detection of contamination but also provided information to help industry avoid violations and improve the overall quality of the product. This educational approach, which has always been coordinated with enforcement of the legal requirements of the food and drug laws, is often unknown to those not fully conversant with the Food and Drug Administration's work.

One of the outstanding personalities in the early food sanitation programs was B. J. Howard, chief of the microchemical laboratory of the Bureau of Chemistry. His applications of the microscope to the detection of decomposed, filthy, or insanitary foods were a major contribution to improvement in the sanitary quality of foods in this country. For the development of a mold count method of detecting rot in tomato products, he received worldwide recognition.

Although the microbiological aspects of food sanitation were an important element of the early investigations, a separate microbiological laboratory was not created in the Bureau of Chemistry until 1913. Under the direction of Dr. Charles Thom, the noted mycologist, the laboratory continued and expanded investigations in food sanitation and spoilage and food poisoning. It was in this laboratory that Dr. Stewart Koser conducted his studies of the metabolism of coliform organisms. His findings form the basis today for distinguishing *Escherichia coli* from other members of this group. Research in food sanitation was further expanded under Dr. A. C. Hunter, who became director of the bacteriology laboratory when the Food and Drug Administration was created in 1927. Drs. Thom and Hunter were authors of the book "Hygienic Fundamentals of Food Handling," published in 1924. It was one of the earliest books, if not the first, on this subject.

Improvements in the Law

The Food and Drugs Act of 1906 defined a food as adulterated "if it consists, in whole or in part, of a filthy, decomposed, or putrid animal or vegetable substance . . . ." This was the legal basis on which the food sanitation programs were founded. Although major improvements resulted from application of this requirement, there was early recognition of serious limitations of the law. This is best summed up by the following statement from the 1933 Report of the Food and Drug Administration by Walter G. Campbell (*1*):

"One of the most serious limitations of the present law, of especial moment where public health questions are involved, is the lack of control of insanitary practices in food-manufacturing plants. Jurisdiction under the Federal statute exists only after a product has been shipped or offered for shipment within the scope of the law. The detection of insanitary practices through inspection in the manufacture of food products does not give sufficient warrant for removing offending goods from interstate channels. To obtain evidence of contamination that will warrant a charge of adulteration within the meaning of the law, it is necessary to collect representative samples of the product and analyze them. This is by no means always an easy matter. Analytical methods have not been developed with that degree of refinement needful to establish in all instances evidences of insanitary handling of a product originating in an insanitary factory."

This important gap in the law was corrected in the Food, Drug, and Cosmetic Act of 1938. It defines food as adulterated—

"If it consists in whole or in part of any filthy, putrid, or decomposed substance, or if it is otherwise unfit for food; or

"If it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or

whereby it may have been rendered injurious to health. . . ."

Other requirements of the 1938 law or its amendments made factory inspection mandatory and extended jurisdiction to articles adulterated while held for sale (whether or not the sale is the first one) after shipment in interstate commerce.

These changes gave the Food and Drug Administration legal authority to deal comprehensively with food sanitation.

Enforcement Procedures

The 50 years of food law enforcement coincides with the period of vast expansion of the food industries. Increasingly, food production has moved to large factories which distribute products throughout the Nation. Often the products have been so altered in form that the consumer has little basis on which to judge their original cleanness and wholesomeness. As the more obvious forms of adulteration disappeared, newer, more subtle forms became apparent. These have required development of new techniques for their detection.

To provide for the most effective and efficient use of the limited funds and facilities available to deal with the increasing needs for consumer protection, the project system of operations was introduced in 1922. In brief, this system consisted in the formulation of a comprehensive and unified plan of operations for the entire field force, directed against specific classes of products that experience had shown to be most likely to be in violation. Priorities were assigned for work allocations in the following order:

1. Violations involving danger to health.
2. Offenses against decency (insanitation, filth, and decomposition).
3. Economic adulteration.

The project system is the basic pattern for the regulatory programs of today, including the programs in food sanitation.

In order to determine the types, sources, and routes of transmission of contamination, a knowledge of methods of production, processing, packaging, and marketing is necessary. This information is obtained through broad investigations of an industry in various localities by inspectors of the field force, usually in collaboration with technical experts from the Washington headquarters. With this background, inspectional and laboratory techniques are devised, policy is determined, and a plan of action is issued for uniform application throughout the country.

The basic operation in a food sanitation program is the sanitary inspection of the factory. The likelihood that food may be polluted or contaminated with filth in the factory is in proportion to the distance between the filth and the product under preparation. The objective of the sanitary inspection is to measure this distance in terms of space, time, opportunity for pollution or contamination, and vehicles of transmission.

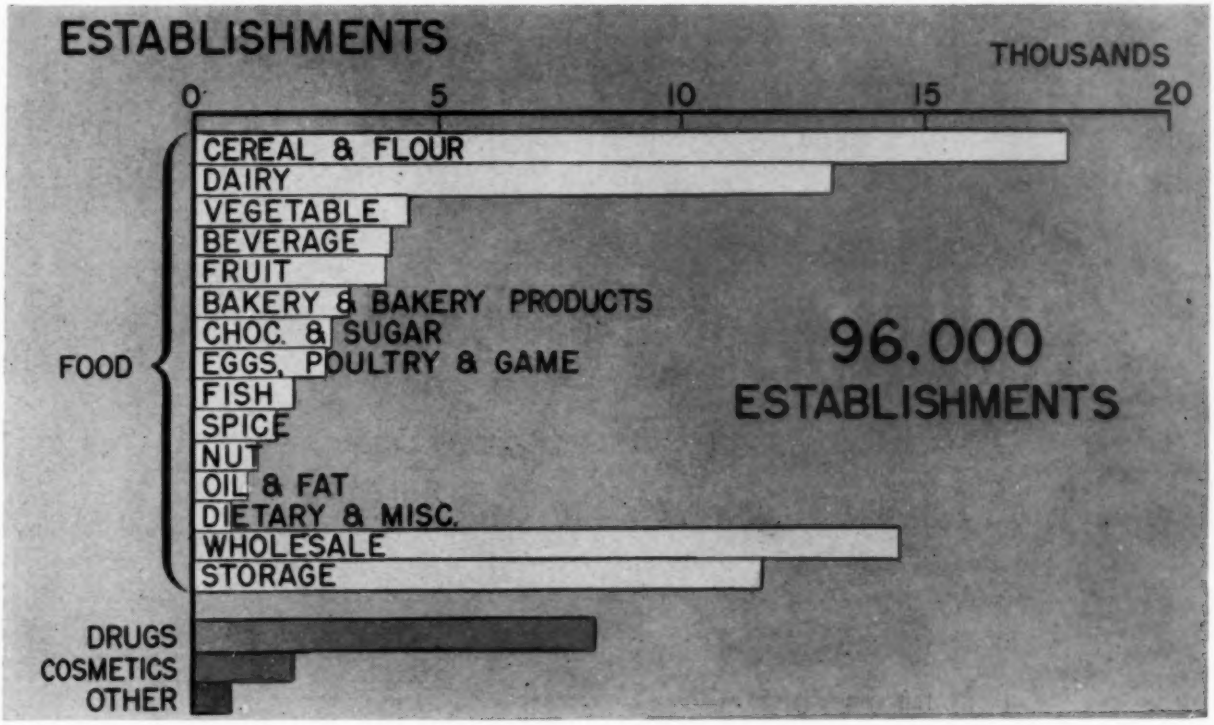
An establishment operating in a manner to invite, or permit, contamination of food with foreign matter properly classified as filth is insanitary. The objectionable matter may be the excreta of man or animal, or it may be flies, maggots, worms, insects or insect parts, rodent hairs, or other such material.

In many instances, the contaminants are macroscopic, and detection of the avenues of their entrance into food depends only on keen powers of observation and common sense. In other instances, the contaminants are micro-organisms or microscopic filth, and knowledge and appreciation of invisible routes of distribution are required.

Sanitary inspection evidence alone, presented in court by the inspector, often with pictures and exhibits demonstrating insanitary conditions, is sufficient to support a charge that the product "may have become contaminated with filth." Such action is essential in instances in which the objective evidence of even gross contamination has been removed or destroyed by such processes as filtration or pasteurization of the product. More commonly, however, insanitary conditions result in contamination that can be detected in the finished product by bacteriological or microscopic examination.

In practice, then, products shipped from an insanitary establishment are usually sampled in interstate commerce for laboratory analysis. The findings may confirm the inspection evidence of insanitation and establish the presence of filth in the product. Offending products

Figure 1. Establishments engaged in distribution of products subject to regulation by the Food and Drug Administration.



may be removed from the market through seizure by the Federal courts, and the shipper may be prosecuted for, or enjoined from, violating the sanitary requirements of the law.

Voluntary Correction

Application of these techniques on an industrywide basis, within the limits of funds and facilities, exerts a strong corrective influence. Correction depends on education, and education is inherent in enforcement of the food sanitation requirements. The basic investigations essential to development of a food sanitation program are usually conducted widely in the affected industry. Methods developed to detect contamination are made available to industry for use in preventing contamination. The food and drug law now requires that the FDA inspector give to the agent in charge of the establishment a written report of conditions or practices that might lead to violations of the sanitary requirements of the law. Prior to this amendment, the inspectors discussed with management any such conditions so that voluntary corrective measures might be instituted.

The Food and Drug Administration also promotes voluntary compliance with the law by such means as talks to trade groups, surveys, consultations, and, whenever practicable, direct assistance in solving technical problems. Punitive action under the law then, falls largely on operators who are careless or who are unwilling to use the measures available to them to avoid violations.

It has been stated that the food and drug laws, and particularly the "insanitary conditions" clause in the definition of adulterated foods, have been major stimuli to improvement in food sanitation (*2*). Certainly this new provision focused attention on a phase of food handling not well attended to by some industries in the past. The response to this provision by the food industries has been gratifying. There are few trade associations or large operators in the food field that are not now active in programs to improve sanitation.

Need for Expansion

Despite the progress that has been made, there is a serious need for expansion of all food

sanitation programs—national, State, and local. As shown in figure 1, there are some 96,000 establishments in this country distributing products subject to the Federal food and drug law, the vast majority of which are in the food field. In addition, food and drug imports are subject to the same requirements. There are sanitation problems of greater or lesser degree connected with all the food commodity groups listed. About 10 percent of the establishments can be inspected and about 7 percent of the imports can be sampled each year with the present staff (fig. 2).

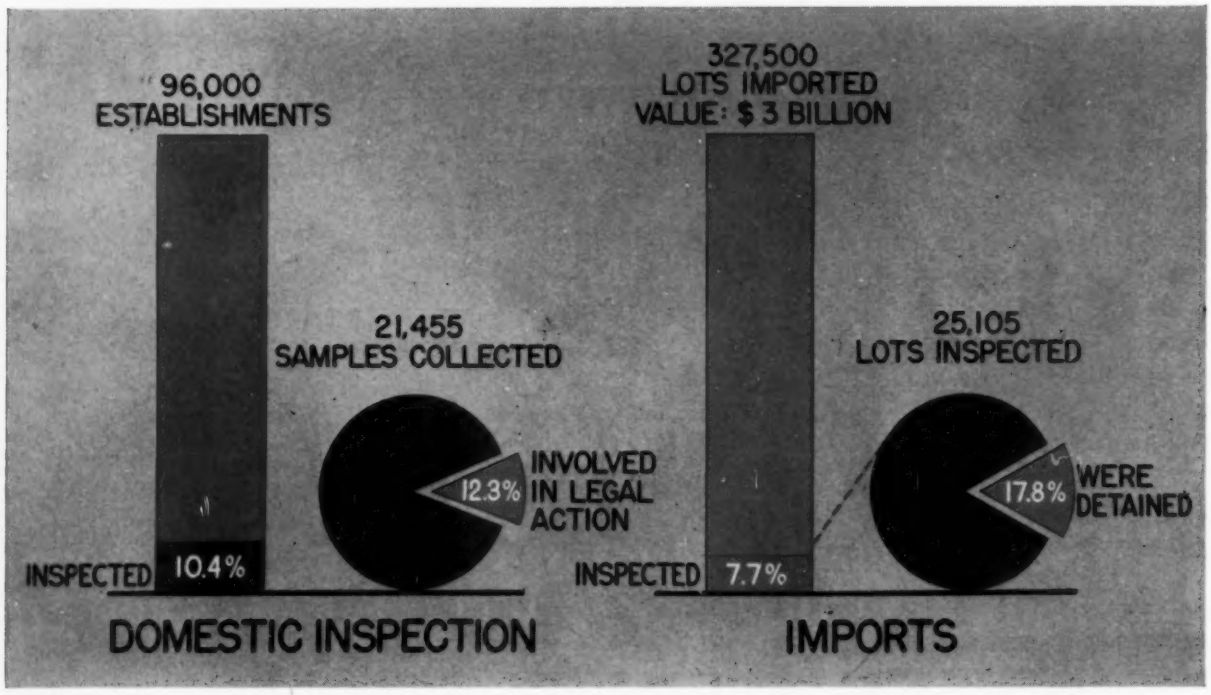
The major food sanitation programs of the Food and Drug Administration have been concerned with certain cereal products, butter and cheese, certain fruit and vegetable products, bakery products, confectioneries, eggs, and certain fish products. Current emphasis is on edible oils and poultry. Many commodities within these groups and others in figure 1 have not received organized action with respect to sanitation.

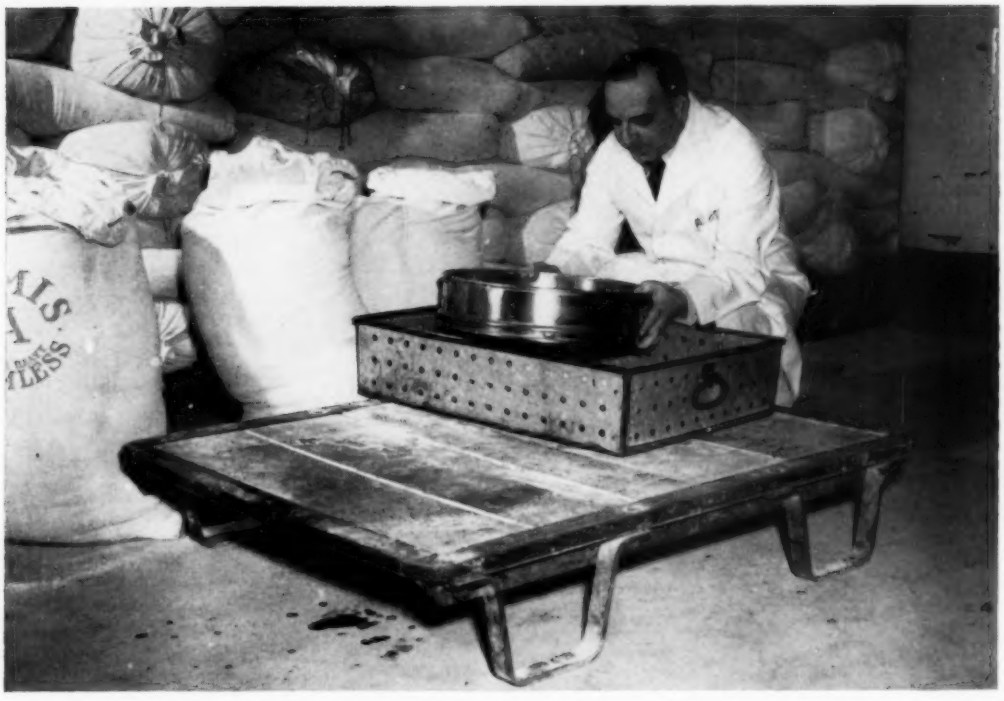
During fiscal year 1955, an average of about 75 tons a week of insect-infested, rodent-defiled, or decomposed food was seized under the food and drug law and removed from trade channels. More than four-fifths of all food seizures fall in these categories. Though a substantial proportion of the food becomes contaminated while it is in wholesale or storage warehouses apart from the point of production, too frequently contamination occurs during production.

Much of the progress in food plant sanitation under FDA programs has been based on the elimination of the more obvious sources of contamination: insects and rodents. Inspection techniques for their detection are relatively simple, and laboratory procedures for the detection and isolation of insect and rodent filth in food have been available for the past 15 years. Emphasis on these factors has encouraged remarkable improvement in (*a*) surroundings, structure, maintenance, and operation of plants and equipment; (*b*) cleanliness and soundness, sorting and storing, of raw materials; and (*c*) plant and laboratory control of raw materials and finished products. It has led to the establishment of sanitary programs as an integral part of food production.

Except in those instances in which contamination with micro-organisms has resulted in clear evidence of danger to health, little has

Figure 2. The scope of accomplishments of the Food and Drug Administration, fiscal 1954.





Bakery warehouse flour being examined by FDA inspector for insect infestation.

been done, or can be done with the staff available, in the bacteriological aspects of food plant sanitation. Foodborne infections and intoxications have not decreased in recent years as have waterborne and milkborne diseases. Much of the foodborne disease probably results from mishandling at the point of consumption. But it may well be that there is more bacterial contamination of foods shipped in interstate commerce than is generally realized. Since the enteric infections transmitted by foods must be regarded essentially as evidence of fecal contamination, the importance of improved sanitation during all stages of food production and handling becomes apparent. A much enlarged complement of microbiologists in the FDA field offices is needed to meet the problems in this area.

The Food and Drug Administration has broad responsibility for the protection of the public against interstate traffic in insanitary foods. As new food products, increasingly in processed ready-to-eat forms, appear on the market, expansion of the Food and Drug Administration of the order recommended by the Citizens Advisory Committee will be necessary to cope with the many new food sanitation problems (*3*).

Many foods, of course, are sold within the community or the State in which they are produced. Sometimes manufacturers having difficulties with the Food and Drug Administration purposefully restrict the distribution of their products to intrastate traffic. Sanitation of these foods is the problem of State and local officials.

Food sanitation, then, is the concern of State and local officials as well as national officials. The combined efforts of all are necessary to afford the degree of protection from insanitary food the consumer expects and is entitled to.

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FDA Nutrition Program

By E. M. NELSON, Ph.D.

The passage of the Food and Drugs Act of 1906, prohibiting adulteration and misbranding of foods, accelerated a consideration of their nutritive value and the advancement of nutrition science. In the first few years of the new law, the adulteration of foods involving the use of poisonous or deleterious ingredients was of primary importance. Foods containing toxic dyes and preservatives were common examples. As adulterated foods of this kind were driven from the market, greater attention was given to so-called economic types of adulteration such as the substitution of non-nutritive fillers, water, or other cheap ingredients for the more valuable food ingredients which the customer expected to find in the foods he purchased.

The knowledge of nutrition in those years did not permit the critical evaluation of the effects of processing and other manufacturing procedures on the nutritive value of our food supply that is commonplace today.

Since 1906, the science of nutrition has advanced more rapidly than in any prior period of time. It was not until the early part of the century that laboratory animals were used in testing the nutritional adequacy of foods. The word "vitamin" was coined in 1911, but it was not until 1926 that products were examined for vitamin content. The isolation, identification, and synthesis of the major vitamins took place in the decade from 1930 to 1940 when the importance of vitamins in our dietary was brought to the fore.

The enactment of the Food, Drug, and Cosmetic Act of 1938 reflected the progress that was being made in the field of nutrition and applied the new scientific knowledge to the protection of consumers. In addition to the basic adulteration and misbranding provisions of the Act of 1906, the 1938 law gave authority to establish legal standards for foods and thus provide for better control of the nutritive value of such products. It required more informative labeling of foods generally and authorized special labeling requirements for foods for special dietary uses.

The policies and regulatory actions of the Food and Drug Administration are designed to provide consumers with the benefits of practical application of reliable nutritional knowledge in the production and labeling of foods, and to prevent consumer exploitation by pseudo-nutritionists and other quacks.

A standard for a food under the Food, Drug, and Cosmetic Act must "promote honesty and fair dealing in the interest of consumers." Under this provision, consideration must be given to the effects of the kinds and amounts of ingredients permitted in a standardized food on its overall nutritional value. This has been of particular significance in considering proposals to add specific nutritive factors such as vitamins and minerals to staple foods.

Fortification of Foods

The Food and Drug Administration has followed a policy that is intended to limit the addition of specific nutritive ingredients such as

Dr. Nelson is chief, Division of Nutrition, Food and Drug Administration.

vitamins and minerals to standardized foods to those instances where there is convincing nutritional evidence that the added nutrients will provide substantial benefits to significant segments of the population.

The addition to foods of specific nutrients already adequately supplied by unfortified common foods is not only wasteful but tends to confuse consumers as to their nutritional needs and the nutritional properties of our food supply.

The need for a basic Food and Drug Administration policy with respect to fortification of foods arose in connection with hearings in 1940 on standards for flour and related products. Many proposals to enrich flour with most of the known vitamins and many minerals were made by various proponents of the flour industry.

The FDA took the position that the addition of a vitamin to flour would not be desirable unless there was evidence that a substantial part of the population consumed a diet deficient in the vitamin in question. Such evidence might be deduced from dietary surveys or from clinical observations with respect to the occurrence of deficiency diseases.

It believed that it was also essential to know whether a food is a suitable vehicle for retention of the vitamin through any processes that may be necessary in preparing the food for consumption. It was important to know too that the fortified product would reach the population that was receiving a diet deficient in a particular vitamin.

If these conditions were met, it was important to add the vitamin in suitable quantities. If flour provided 25 percent of the calories ingested, it seemed proper to require that the quantity of flour consumed daily should contain at least one-fourth of the daily requirement of the vitamin used for fortification. There seemed to be no purpose in adding more than the daily requirement to this quantity.

The principles stated at the 1940 hearings have been generally accepted as the basis for fortifying flour. They have been used as a guide in subsequent proposals to fortify other foods, and they have received support from the Food and Nutrition Board of the National Research Council.

In accordance with a basic policy, legal standards for the following staple foods, containing added nutritive ingredients, have been established:

Enriched flour.
Enriched bread and rolls.
Enriched macaroni products.
Evaporated milk with increased vitamin D content.
Oleomargarine with added vitamin A.
Enriched corn products.

Standards for the same kind of foods without fortification have also been established. It will be noted that the Federal law does not require enrichment of these foods but leaves to manufacturers and consumers the freedom of choice to select the type desired. A schedule of sampling these standardized foods for vitamin, mineral, and other types of examination to determine compliance is a part of FDA regulatory operations.

Some Regulatory Programs

The degree of attention given to specific types of products will vary from year to year, based on experience and need for broader or more restricted coverage. Regulatory programs have also been developed to provide for the selective sampling for laboratory examination of the numerous vitamin and mineral supplements and other foods for special dietary uses. Since the facilities for laboratory examination of products bearing vitamin and other nutritional claims are limited, other regulatory programs have been developed to protect consumers from exploitation through false and misleading nutritional and therapeutic claims for such articles. These projects are designed to deal with representations which are unwarranted regardless of the nutritional properties of the particular products involved.

Misrepresentations concerning foods, and particularly vitamin and mineral preparations, are a difficult problem for the Food and Drug Administration. Much misinformation has been furnished the public about nutrition and its relation to health. Some of this stems from competition and attempts to gain a sales advantage through advertising and other promotional material based on recent scientific discoveries of undetermined or unestablished

significance. The substantial contribution to consumer misinformation and deception made by nutritional quacks and faddists cannot be overlooked.

An intensified program of consumer education by all those in a position to furnish scientifically sound information about nutrition is necessary to increase the effectiveness of the various Federal and State laws designed for consumer protection in this area.

The broad statement that the food of the American people does not furnish a satisfactory diet is frequently made. The contention is that our soils have been so depleted that they can no longer produce plants of adequate nutritive value or that chemical fertilization of crops has resulted in reduced nutritive value.

These pseudo-scientific statements have an aura of plausibility but little scientific justification.

To only a very small extent is the composition of the parts of plants that people eat governed by the composition of the soil. The composition of the plant and its nutritive properties is controlled primarily by genetic factors which also control its size and shape. Much is made of the destruction of vitamins in cooking and loss of vitamins and minerals when the water in which foods are cooked is thrown away. To be sure, there are losses of this kind, but the facts have been greatly overemphasized. Such losses have been greatly reduced by improved methods of cooking. One must remember that man began cooking his food a long time ago.

Nutritional deficiency diseases in the adult generally result from restricting the diet to a single food or to a very few foods rather than cooking losses. In the Orient, beriberi occurs among populations confined principally to a diet of polished rice. Pellagra and riboflavin deficiencies were observed in the southern part of this country, largely among people whose diets were restricted by their economic status to cornmeal, fatback, and molasses. Their diets have been improved both by changed economic conditions and by a food enrichment program with the result that vitamin deficiency diseases are now rarely seen in this country.

The similarity between the symptoms observed in human beings and other animals suffering from nutritional deficiencies and those resulting from non-nutritional causes has provided another fertile ground for exploitation of the consumer.

The extremely low incidence of demonstrable nutritional deficiency in this country has made it necessary for those with products to sell to talk in terms of "subclinical deficiencies" which, in less elegant language, means that the condition so described cannot be demonstrated to be of nutritional origin. This device, coupled with statements about the unreliability of our common food supply as a source of nutrients, because of soil erosion, cooking losses, and other similar misrepresentations, is typical of the misuses in which modern nutritional knowledge is being employed.

Foods for Special Dietary Uses

The Food, Drug, and Cosmetic Act recognizes the difficult and technical problems in the labeling of vitamin preparations and foods used in the management of disease. Section 403 (*j*) of the act gives the Secretary of the Department of Health, Education, and Welfare power to promulgate regulations to cover the labeling of those products. It also requires that the labels of vitamin preparations show the vitamin content. Section 403 (*j*) reads:

"A food shall be deemed to be misbranded if it purports to be or is represented for special dietary uses unless its label bears such information concerning its vitamin, mineral, and other dietary properties as the Secretary determines to be, and by regulation prescribes as, necessary in order fully to inform purchasers as to its value for such uses."

Biochemists generally regard vitamins as foods since they are essential nutrients, needed for growth and maintenance of the body. Only minute quantities are needed daily. Since pharmaceutical manufacturers have equipment and personnel trained to handle such small quantities, vitamin preparations ordinarily fall into drug channels for distribution and marketing.

Vitamins are usually measured in units, milligrams, or even micrograms—terms unfamiliar to many laymen. To meet the requirements that labeling for foods for special dietary use must fully inform the purchaser, "minimum daily requirements" have been established for vita-

mins. The vitamin content of a preparation must be stated on the label in terms of the proportion of the minimum daily requirement provided in the recommended daily intake. The quantities of the four minerals, iron, calcium, phosphorus, and iodine, which before 1940 were the most frequently used supplements to the daily diet, must also be declared in the same manner.

Infant foods must be labeled to show all ingredients. Since the feeding of infants often presents problems, it is important that infant foods bear all the information necessary for their use. Labels of other foods are not required to name the spices, flavorings, or coloring material present. The label of a product that is a complete or partial substitute for human milk must state that additional quantities of vitamins C and D and of iron must be supplied from other sources if the quantities present are not adequate. The label must bear a quantitative declaration of vitamins A, B_1, C, and D, and must list the percentages by weight of water, protein, fat, available carbohydrates, crude fiber, calcium, phosphate, and iron.

Many foods are offered for control of body weight, particularly by reducing. The label of a food for the control of body weight or the dietary management of disease must state the percentages by weight of protein, fat, and of available carbohydrates as well as the number of available calories in a specified quantity.

If crude fiber is represented to be of significance in a food, the percentage by weight must be declared on the label. If saccharine or a saccharine salt is used in a food in lieu of sugar, the label must bear the statement, "Contains -- saccharine (or saccharine salt, as the case may be), a non-nutritive artificial sweetener which should be used only by persons who must limit their intake of ordinary sweets." The weight of saccharine or saccharine salt is inserted in the blank.

If a food is for special dietary use because of reduced allergenic properties, the label must bear the common or usual name of each ingredient, including any spice, flavoring, or coloring used. The label must also contain a statement indicating the nature and effect of any process to change the allergenic properties of the food or its ingredients.

All of these requirements are contained in the food and drug regulations promulgated in 1941. The regulations have served their purpose well, but now they are somewhat outdated and in need of revision and extension.

A few years ago the labeling of foods with reduced sodium content became an important problem. It was shown that a reduced sodium intake was more important in the control of blood pressure than had been realized. Many foods on the market labeled "No salt added" contained considerable quantities of sodium from other sources although it was a statement of fact that no salt had been added. Some contained considerable amounts of sodium as a natural constituent. Sodium glutamate, which is used extensively for flavoring, and sodium propionate, which is an effective mold inhibitor, may contribute unsuitable quantities of sodium.

Foods labeled "No salt added" are attractive to a person seeking low sodium foods, but they have little value for the purpose desired. Such representations are, of course, misleading. There are a number of ways in which foods may pick up sodium in the process of manufacture, and producers of foods that are offered for the benefit of persons on a low sodium diet should determine the actual sodium content of the food.

The regulations require that if a food is represented to be of value because of a low sodium or low salt content, it must be labeled to show its sodium content in milligrams per hundred grams of food as well as per serving.

The Division of Nutrition

The Division of Nutrition of the Food and Drug Administration is responsible for the development of scientific facts and opinions concerning nutrition as a basis for the policies and regulatory activities of the FDA. It also examines official samples for vitamin or other nutritional properties, by means of biological, microbiological, or chemical procedures which cannot be performed in the field laboratories of the FDA.

Under normal circumstances, the division's work is about equally divided between strictly enforcement operations and specialized research designed to facilitate or improve FDA enforcement of the Federal Food, Drug,

and Cosmetic Act. Research activities of the division have been limited almost entirely to the development or improvement of assay procedures for enforcement purposes. There is little incentive to do this kind of research in other nutrition laboratories. Such research has made possible a more rapid and precise examination of a greater number of samples without an increase in manpower.

The manufacturers of vitamin preparations have a very similar problem, and there has been excellent cooperation with industry laboratories in the study and development of control methods.

It is necessary that the Division of Nutrition keep abreast of the scientific developments in the field of nutrition. This is accomplished by a study of the scientific literature, communications and consultation with outside authorities in the field, and by attendance and participation in the activities of scientific societies and associations. It must also be alert for developments in manufacturing and labeling practices which may require changes in policies and regulatory activities in order to recommend such changes to the Commissioner of Food and Drugs.

In the case of litigation involving products examined in its laboratory, the division must be prepared to provide convincing scientific evidence of the deficiency suitable for presentation in the Federal courts. The division's analysts who are called upon to provide such testimony must be so qualified by training and experience that their evidence can successfully withstand cross examination.

In cases involving false and misleading claims about the nutritive or therapeutic value of vitamins, minerals, and other food factors, various members of the Division of Nutrition are called upon to testify as experts and must therefore be prepared to qualify as such in court. Among other things, they must have a comprehensive knowledge of the views of other experts in the field so that they may testify as to what constitutes the consensus of scientific authorities in the field of inquiry. Such qualifications are likewise of utmost importance to the work of the Food and Drug Administration, to the end that its actions and policies will be in accord with the best scientific knowledge available and enjoy the support of the outstanding authorities in the field of nutrition.

Fourth Annual Symposium on Antibiotics

The Fourth Annual Symposium on Antibiotics, sponsored by the Division of Antibiotics of the Food and Drug Administration, Department of Health, Education, and Welfare, with the journals, *Antibiotics and Chemotherapy* and *Antibiotic Medicine & Clinical Chemotherapy* will be held on October 17–19, 1956, at the Willard Hotel, 14th Street and Pennsylvania Avenue, NW., Washington, D. C.

To allow the program committee time to review material for presentation and to facilitate publication of the Antibiotics Annual 1956–57, manuscripts must be submitted by September 17, 1956.

For further information, address Dr. Henry Welch, director, Division of Antibiotics, Food and Drug Administration, Washington 25, D. C.

New Problems of Food Safety

By FRANK A. VORHES, Jr., B.S., and ARNOLD J. LEHMAN, M.D., Ph.D.

The safety of food has been of concern to man from the very earliest times. Whether through instinct or intelligence, by trial and probably sometimes fatal error, forgotten benefactors of the race must have learned to eat substances that would not harm them; and they must have conveyed that knowledge to others, else we might not be here to speculate in this vein. Though probably accumulating slowly, a wealth of information regarding food safety had developed by the dawn of recorded history; witness, dietary customs and taboos reflected in the most ancient of ecclesiastic law.

With a few exceptions, those substances, natural or unnatural, that result in immediate acute harm are not the cause of food safety problems in modern civilization. Rather, it is the insidious hazard of chronic toxicity that is the most serious concern today, a hazard that demands a far more subtle and searching approach.

Current food safety problems arise in large part as a result of technological progress in food production, processing, and distribution. To meet economic pressures, the agriculturalist, that traditional conservative, must now intensively apply many types of advanced technology. His partner in "agribusiness," the food processor, is, of course, no novice in this field. Their joint accomplishment during the past several decades is abundantly apparent in the ample quantity, high quality, and appetizing variety of foodstuffs available to the American public. Nonetheless, in the very nature of the progress that has brought these benefits, hazard to food safety is inherent. That fact does not necessarily mean that harm is actual or even imminent; but it does mean that need for gauging the existence and immediacy of danger is genuine and pressing.

One important group of current food safety problems stems from employment, in food production, of a long and lengthening series of chemical adjuvants—insecticides and insect repellants, fungicides, herbicides, defoliants, plant growth regulants, animal growth stimulants and medicaments, crop protectants and fumigants. These substances are commonly of complex, sometimes uncertain, and even occasionally unknown chemical identity. One of the problems in this area is to ascertain whether food exposed to them is contaminated and to gauge the degree of contamination.

In processing, food may receive preservatives, antioxidants, colors, bleaches, flavors, coatings, drying agents, moistening agents, thickening agents, sequestering agents, "aging" agents, stabilizers, emulsifiers, neutralizers, acidifiers, sweeteners—in short, retainers, modifiers, and inhibitors of virtually every property natural food may exhibit. (But we don't mean to imply any opposition whatever to genuine improvement per se.)

Associated with food production and processing are new equipment cleaners, sanitizers, and lubricants, new surfacing materials, and new alloys composing the equipment itself, any of which may get into the product.

Mr. Vorhes is chief of the Division of Food, and Dr. Lehman is chief of the Division of Pharmacology, Food and Drug Administration.

Today's food packages, incorporating new plastics, enamels, films, and tissues, with their own plasticizers, antioxidants, catalysts, impregnants, coatings, and the like, are still another potential source of additives to the very food which these materials are intended to protect from contamination.

Some anonymous philosopher has said that he who can get a corner on a food production adjuvant, used in even relatively minute quantity in this multibillion-dollar commerce, has his fortune made. Indeed, the benefit to their sponsors seems likely to prove the only net advantage of some proposed food additives. But we need not consider those wholly undeserving suppliants for entry into our food supply. Nor need we concern ourselves with most of those natural substances that have been tested through long years of use. Entirely aside from these, the novel and substantially artificial food additives that may be conceded some real functional merit are so many that an informed observer has no doubt whatever that they present food safety uncertainties. It is estimated that some 25,000 chemical additives have been considered for use in food since 1940 (see chart).

Safeguarding the Physically Subnormal

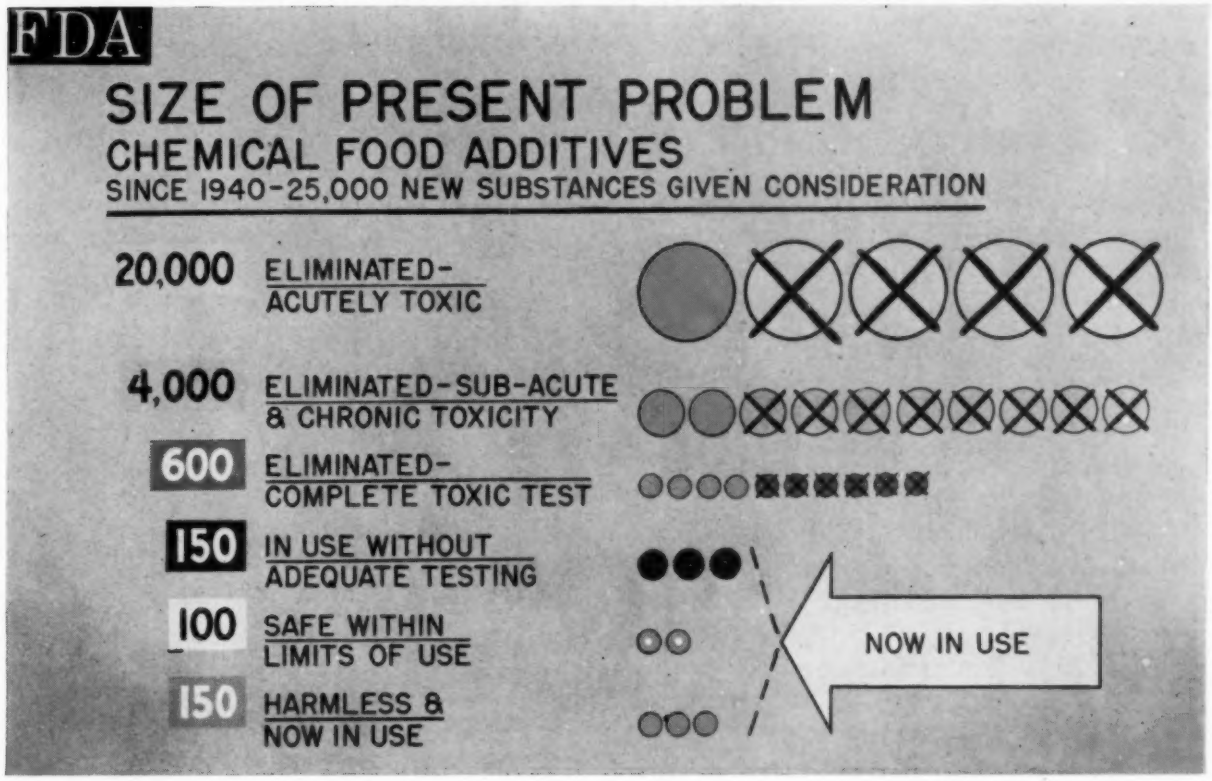
Set aside for the moment (but don't forget) the fact that there is a large and growing backlog of study to ascertain food contamination from its production and processing adjuvants and to evaluate the toxicity of the adjuvants to normal adults in good health. Aside from that aspect, it remains generally to be determined what their effect may be on persons in subnormal physical condition.

No person is expendable within the meaning of the Federal Food, Drug, and Cosmetic Act. In a very significant decision (233 U. S. 399), the Supreme Court said that the food at issue "may be consumed . . . by the strong and the weak, the old and the young, the well and the sick; and it is intended that if . . . because of any added poisonous or other deleterious ingredient, [it] may possibly injure the health of any of these, it shall come within the ban of the statute."

Orthodox techniques and procedures of toxicology are not well suited to establishing that a substance is safe for persons with varied types of physical impairments. Pharmacological investigation ordinarily proceeds on the basis of observable effects produced by administering the test substance to cloistered, well-fed and well-cared for, normal laboratory animals. However appropriately the findings so obtained may be interpreted in application to the human norm, there may be valid reservations to translating them into terms of effect on health of unusually susceptible individuals. The Supreme Court decision cited allows those responsible for safeguarding the food supply scant liberty to indulge in the educated guess or the calculated risk.

This consideration comes to a particularly critical focus with respect to milk, which may represent the principal component of the diet of babies, old folks, and invalids. The law authorizes establishment of tolerances for residues of useful pesticides "to the extent necessary to protect the public health." One may not assume that pesticides don't get into milk merely because no one purposefully puts them there. Pesticides are useful in production of feed and fodder crops, on dairy premises, and on lactating animals themselves. Some of them, particularly some halogenated hydrocarbons, when ingested or absorbed through the skin of animals, are known to appear in the milk—sometimes unchanged, sometimes modified by reaction within the animal system. One must consider whether residues of other pesticides so employed may perhaps have escaped detection in milk because the parent compound metabolizes to another toxicant unresponsive to methods of analysis so far employed. Under these circumstances there may be only an obscure basis, generally, on which to set tolerances for residues of pesticides used in connection with milk production.

The possibility exists, of course, that use of a pesticide would not contribute contamination to milk, but this raises other quite practical questions. For example, how does one ascertain that no residue whatever is present in a food? By analysis? That tool of science is designed to determine the presence of a substance, not its absence. It is capable of demonstrating some minimum concentration of a specific entity, such minimum being fixed by the limit of



delicacy of the analytical procedure. It cannot show, at least not directly, whether a lesser concentration exists or whether some substance unresponsive to the method is present. Before an adequate method of analysis can be selected or devised, a decision must be reached as to what concentration is of minimum significance, a decision that is practically equivalent to establishing the threshold of contamination. So one may be right back at the starting point. A gauge of harmfulness of the pesticide to the more susceptible segments of the population is ordinarily basic to justification of use of any pesticide, whether it is directly or indirectly associated with dairy practice.

The Biochemical Approach

We cannot offer solutions to these problems, but we can suggest that an improved understanding of reactions that food additives may undergo in the animal (and human) system would contribute substantially. Were it possible to predict the character and extent of biochemical reactions that may cause harm, together with the reactions fostering protection and recovery, not only would toxicological observations be most usefully supplemented, but uncertainties of analytical procedure might also be clarified. The first step would be to ascertain the route and fate of the ingested food additive. This may seem elementary, but such approach has too often been ignored or has been given but scant consideration. Application of the biochemical approach in the study of pesticides that inhibit cholinesterase activity furnishes a relatively recent and encouraging example of its value. At feeding levels much below those resulting in minimal tissue abnormality, these substances have been shown to lower, drastically, the activity of the important body enzyme, cholinesterase. Techniques by which this more delicate index of their harm was established have been adapted to methods of measuring the concentrations of their residues.

Some verbally resourceful investigator, seeking to explain the unexplainable, invented the term "subclinical symptoms." We are indebted to him for expression of a concept pertinent to food safety problems. The specter of as yet unmanifested harm from food additives may

not safely be laid to rest in routine fashion; and it may become a quite personal threat. Most of us have children; some have dependent invalids; many have grandparents; and all may hope to join the ranks of elder citizens. For any of these the ghost of subclinical symptoms may materialize, with tragic consequence, unless understanding of effects of food additives can keep pace with their increasing usage.

Another of the food additive problems, one that is virtually untouched by investigation, concerns the number and variety of the substances in use. In the aggregate they represent almost infinite possibilities for combinations of novel substances in the human diet. It seems hardly conceivable that there would not be some in which the effect of combined toxicants would be not only additive but synergistic.

Obviously, progress in exploring this problem by hit or miss testing of each possible combination, in a sufficient range of relative proportion, could be far beyond any foreseeable resources. However, improved understanding of biochemical reactions might go far in expediting useful findings. At least some examples of the phenomenon of synergism may reflect only associated biochemical reactions in which one agent reacts to produce the primary harm, while another impedes normal resistance or recovery mechanism. If this be even a rough explanation of synergism, quite unanticipated consequences could arise from combinations of toxicants, each present at a level which by itself would warrant no concern.

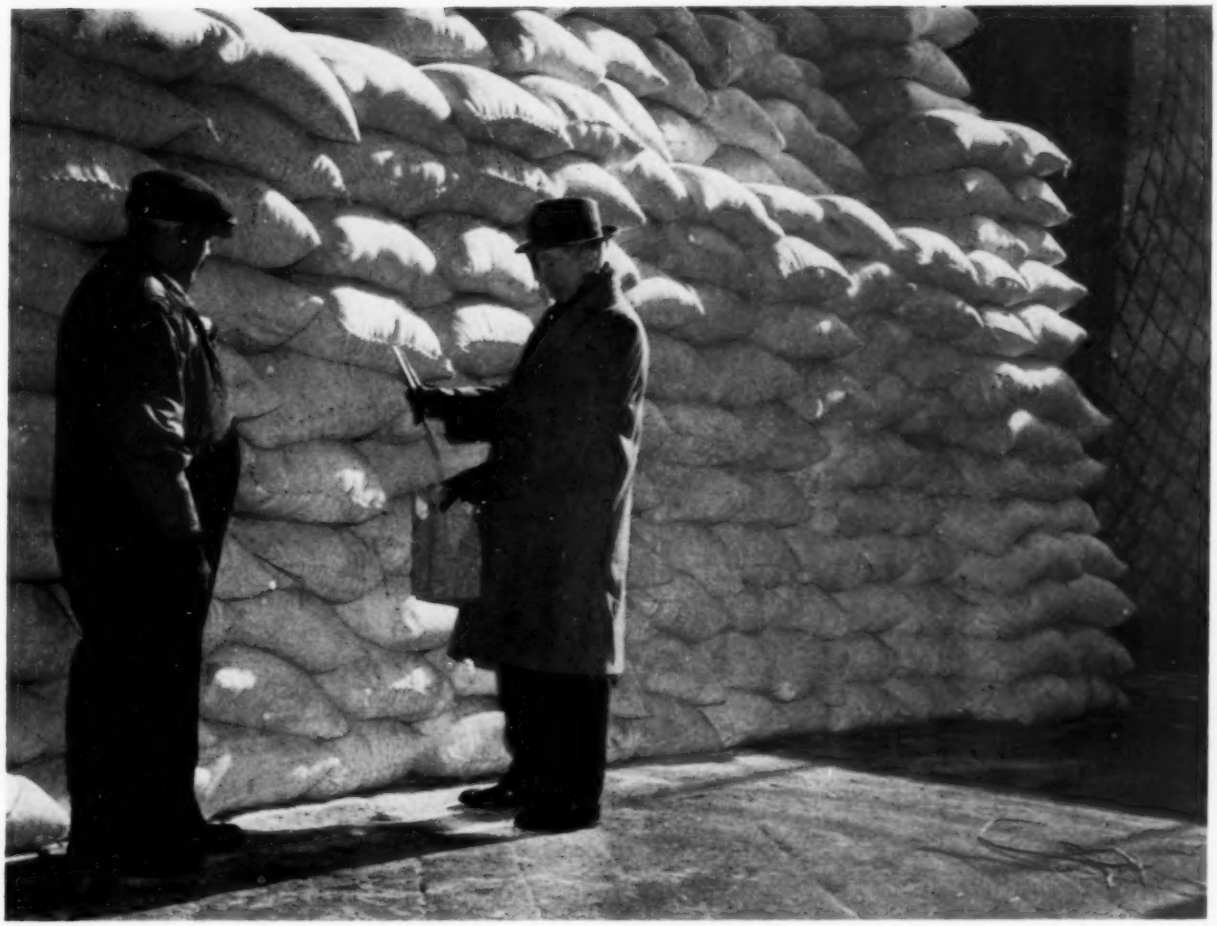
Cold Sterilization

It would hardly be possible, these days, to discuss food-safety problems without bringing to mind those that could conceivably stem from what many informed food technologists believe to be a promising application of atomic energy, that is, so-called cold sterilization. This is accomplished by exposure of food to ionizing rays, either gamma rays, which are not basically different from the more familiar X-rays, or beta rays, which are simply fast-moving electrons. Nothing of significant substance is added to the food so processed; energy alone is imparted to it. Energy in this form produces in organic matter the effect of ionization. Ionization is a molecular change that increases chemical reactivity. Consequently, chemical reactions occur in food as a secondary result of its irradiation. One product of such reactions is peroxide, not only the simple and familiar hydrogen peroxide but peroxides of other kinds, perhaps including those of most complex molecular structure. There is yet no assurance, and it is theoretically improbable, that reactions occurring are solely those producing peroxides. On the contrary, at this stage it appears more likely that the induced reactions are substantially heterogeneous rather than specific.

We disclaim any special knowledge in this area. Although the Food and Drug Administration has not hesitated to cooperate in an advisory capacity on questions within its competence, its responsibilities do not ordinarily extend to active participation in development of new processes. But new processes for food invariably pose potential food safety problems, and, accordingly, the agency always has been an interested observer of such developments.

We were reasonably well assured quite early, from information we received, that there was very remote possibility, if any, of inducing radioactivity in food by exposing it to such levels of radiant energy as are at all likely to become available, or even practicable, for such use. There has been no serious proposal whatever for the direct addition of radioisotopes to food. Radioisotopes, if used in cold sterilization, would be used solely as sources of radiant energy. Actually, at least some investigators of cold sterilization appear to favor mechanical generation of the energy, as more practical than deriving it from radioisotopes. There is room for appropriate concern, of course, that disposal of atomic wastes could result in contamination of water supplies and thereby introduce a threat to safety of the diet. Precautions so far taken, and realistically to be expected, appear to foreclose any immediate prospect of food hazard from such source. However, it will take constant vigilance to maintain that satisfactory situation.

Development of cold sterilization thus far has shown no essentially new or mysterious type of food safety problem. The energy, the application of it, and the mechanism of its



FDA inspector collecting import sample of meal at pier.

effect are new; but the end result seems to be of a quite familiar nature—the appearance in food of new and largely unknown chemical substances. Although probably much more complex, the problem seems basically of the same kind as those stemming from use of new chemical adjuvants in food production.

Radiant energy holds promise of production practicability for such objectives as preventing the sprouting of potatoes, killing trichina organisms in pork and insects infesting grain, pasteurizing a variety of foods sufficiently to extend their life very substantially without refrigeration, and retaining prominent elements of freshness in meat and other commodities.

Energy requirements for accomplishing these purposes vary. Sprouting of potatoes, for example, is inhibited at relatively low energy input; sterilization of micro-organisms generally requires almost 10 times as much. As energy requirements increase, so do unfavorable side effects. The process is not promising for milk, for example, because of disagreeable flavor changes produced by energy input far lower than enough to pasteurize. Nutrient values are also affected at energy input sufficient to sterilize. Vitamins A, thiamine, riboflavin, pyridoxine, B_{12}, ascorbic acid, and niacin are destroyed in varying degree, and some alteration in nutritive value of protein has been observed.

The observed organoleptic and nutrient changes in products subjected to cold sterilization confirm that expected chemical reactions do take place. They signify the possibility, if not the probability, of a wide variety of reactions and, hence, a wide variety of end products. Common prudence dictates a concern as to the identity of such end products. These are food additives, for all practical purposes. Good practice in toxicological investigation involves

feeding of experimental animals at a high level of a proposed food additive, with the objective of discovering the nature of definable injury, a middle level which may or may not give evidence of injury, and a lower level which does not affect the animal. The data so obtained permit an estimate of the margin of safety of the additive in use. Sole reliance on findings of orthodox toxicological study of irradiated foods themselves, in ignorance of both the identity and quantity of substances therein that may influence such findings, invites valid reservations to any final conclusions.

It can hardly be overemphasized that the problem of appraising the safety of cold sterilization is complex, of wide scope, and demanding of very considerable investigative resources. A great deal of work has been done on it, and significant progress has been made. It does not appear, however, that the safety of the process is anything like as near being established as is its production practicability.

Antibiotics as Adjuvants

One class of potential food production adjuvants that does not currently constitute a problem in the same sense as the others discussed is the antibiotics. We have a sufficient gauge of their deleterious properties to conclude that, in food as consumed, their presence in virtually any concentration whatever is unjustified.

The wide and valuable usage of antibiotics in medicine is well known. The reasons for their curative efficacy are precisely the reasons that make them effective preservatives: They combat development of bacteria, the prime cause of food spoilage. It is not so generally appreciated that their medical usage is attended by distinct hazard of sensitization, varying in degree with different antibiotics. To the individual who is or has become sensitized, administration of an antibiotic may cause serious illness or even death. A method of developing sensitization is by administering the agent in small repeated dosage, in a manner paralleling that of repeatedly ingesting food preserved with an antibiotic. The use of antibiotics as food production adjuvants in ways such that they actually are consumed is therefore manifestly contrary to the public interest, and the Food and Drug Administration has formally so declared.

However, there are a few justifiable uses of antibiotics in food production or processing. For example, it has been shown that fresh dressed chicken cooled in ice water containing 10 p.p.m. chlortetracycline will not absorb more than 7 p.p.m. of the antibiotic in any portion of the flesh, and that more than 99 percent of this pickup will be destroyed by any type of cooking sufficient to make the chicken suitable for consumption. The cooked treated chicken exhibits antibiotic activity no greater than that of untreated chicken. On this evidence, a tolerance of 7 p.p.m. of chlortetracycline, not to be exceeded in any part of the flesh, has been established for raw chicken.

Conceivably, there may be other, equally safe, food uses of antibiotics, but they would need to be equally well supported by fact in each case. It seems improbable, at this time, that many such instances could arise.

Summary

Chemical additives, whether they be intentionally put into food or the incidental result of food production or processing procedures, are today the major cause for concern with respect to the safety of food. And it is the uncertainty surrounding these substances and their effects rather than any knowledge of actual harm that is the main reason for concern. In particular: What are the effects on persons with physical impairments? What are the effects of the multitude of combinations of the many substances in use?

In discussing any problem without at the same time describing measures taken toward its solution, or ancillary controls in effect pending final solution, it is difficult to avoid exaggerating the immediacy of evils the problem may involve. We have no wish to be alarmists. Our purpose has been to examine objectively some of the elements of needed knowledge that would contribute to understanding food safety problems.

Control of Pesticides on Food

By WINTON B. RANKIN, M.S.

Pesticides are today considered essential for the production of an adequate, high quality food supply. But pesticides are poisons, and some of them, if not used properly, may leave harmful residues in or on food. In fulfilling its responsibility to protect the public from the addition to food of poisonous or deleterious substances, the Food and Drug Administration is therefore concerned with pesticides. Its objective is to limit pesticide residues to amounts that will be completely safe for consumption. It is concerned primarily with the possibility of chronic poisoning, rather than of acute poisoning, since the quantities of residues are ordinarily minute.

In accomplishing this objective, the Food and Drug Administration establishes tolerances for pesticide residues; that is, it sets the amount that may remain legally on crops shipped in interstate commerce. Establishment of a tolerance means that the pesticide can be employed usefully in agriculture, that residues within the tolerance are safe, that when the pesticide is used properly it will leave residues that are within the prescribed limit, and that crops shipped in interstate commerce shall not bear residues exceeding the prescribed limit. FDA may exempt a pesticide from the requirement of a tolerance if it finds that the pesticide will not leave poisonous residues.

Mr. Rankin is assistant to the Commissioner of Food and Drugs in charge of the pesticide chemicals program. He has been with the Food and Drug Administration since 1939.

The first regulations listing formal tolerances for pesticides were issued in March 1955. These tolerances were set under a public hearing procedure that required the Department of Health, Education, and Welfare to determine not only what level of residue is safe, but also that the pesticide is necessary in the production or handling of crops. This procedure was not particularly satisfactory to anyone. It was cumbersome and it required a health agency to make agricultural decisions.

Today, tolerances are established under a Federal law enacted in 1954, the pesticide chemicals amendment to the Federal Food, Drug, and Cosmetic Act, also known as the Miller amendment. This law provides new, more convenient procedures for determining how much poisonous agricultural spray or dust may remain safely on crops. It recognizes that sprays and dusts are necessary to insure a continuing supply of high quality foods, and it is designed to permit the effective use of these materials without hazard to the consumer. It assigns agricultural functions to the Department of Agriculture and health functions to the Department of Health, Education, and Welfare. It does not, however, make any change in the basic requirement that foods in interstate commerce shall be free of dangerous quantities of pesticide residues, which is a part of the Federal Food, Drug, and Cosmetic Act.

The new law provides that, within its jurisdiction, a raw agricultural commodity shall not be marketed if it bears a residue of a pesticide chemical, except under one of the following conditions:

1. The pesticide chemical is generally recognized by experts as safe.

2. The Government has established a safe tolerance for the residues of the pesticide chemical, and the residues remaining on the food are within this tolerance.

3. The Government has exempted the pesticide chemical from the requirement of a tolerance.

(For practical purposes a raw agricultural commodity is a crop as it is harvested, and a pesticide chemical is a substance that will destroy or control pests such as insects and weeds. More exact definitions are given in the law itself.)

How the Law Works

There are three principal steps leading to the establishment of a tolerance under the new law:

1. A manufacturer of a pesticide (or any other interested party) submits a petition to the Food and Drug Administration requesting the establishment of a tolerance, a copy of which he sends to the Department of Agriculture requesting certification that the pesticide is useful for the purpose for which a tolerance is sought. In the petition, he must supply information about how he proposes to use the pesticide, the quantity of residues that will remain on the foods, and the toxicity of the residues when they are consumed throughout the life of test animals, such as rats or dogs.

2. Department of Agriculture scientists determine whether the pesticide is useful in agriculture when employed as proposed by the petitioner. If they find that it is, the Department transmits to the Food and Drug Administration a certificate of usefulness and also its estimate of the residues that are likely to remain on the foods.

3. Food and Drug Administration scientists study the experimental data given in the petition and all other available information, including that from the Department of Agriculture. On the basis of this study, FDA establishes a tolerance that meets both the requirements of safety and the needs of agriculture. The tolerance is set forth in a regulation published by the Commissioner of Food and Drugs. Residues within this amount may legally remain in or on the crops to which the tolerance applies.

The same procedure is followed in exempting a chemical from the requirement of a tolerance.

Thus far, formal tolerances or exemptions have been established for almost 100 pesticide chemicals. When the Miller amendment becomes fully effective on July 22, 1956, all pesticides will fall in one of four classes:

Safe chemicals. These may be used without a tolerance or an exemption, because they are not considered poisonous as used on crops. Sulfur, lime, and lime sulfur are in this group.

Chemicals exempted from the requirement of a tolerance. These are considered poisonous, but they are exempted for use on growing crops because excessive or harmful residues will not occur when they are so used. Many copper compounds and pyrethrins are among the materials in this group. (As yet, no pesticide has been exempted for postharvest use.)

Chemicals with a zero tolerance or its equivalent. Some of these, such as mercury- and selenium-containing compounds, are so toxic that no residue whatsoever should remain on food as it is marketed. Others in this group have not been studied enough to show whether they deserve a higher tolerance. Still others, such as tetraethylpyrophosphate, can be employed usefully in agriculture without leaving residues at harvest time. Any pesticide not specifically included in another group has the equivalent of a zero tolerance.

A zero tolerance does not mean that the chemical is barred from use in agriculture; it means that it must be used in such manner that no residue will remain when the crop is shipped.

Chemicals with tolerances higher than zero. Tolerances higher than zero have been set for numerous chemicals which are safe if the residues are kept within a certain limit but which are not safe for uncontrolled use. The tolerance for a chemical applies only to specific crops. The fact that a tolerance is in effect for one crop does not mean that residues of the same chemical may remain on another crop.

According to the Federal Insecticide, Fungicide, and Rodenticide Act of 1947, all "economic poisons" must be registered with the Department of Agriculture before they are shipped in interstate commerce. The directions for use on labels of pesticides thus registered should yield crops with residues within the tol-

erances set by FDA. Growers, therefore, have one simple rule to follow: They should use pesticides according to the label directions—on the crops specified, in the amounts specified, and at the times specified.

Enforcement Procedures

The Food and Drug Administration enforces the Federal law with regard to pesticide residues on foods as follows:

Before the growing season, it studies new developments with regard to pesticides and new recommendations in spray schedules issued by the State agricultural authorities. During the growing season, FDA inspectors keep in touch with State authorities and growers to determine what sprays and dusts are used and how. The inspectors may pick up a few samples from farms, shipping points, or produce markets for laboratory examination to determine the accuracy of earlier tentative conclusions about the quantity of the residues remaining.

When the inspectors visit a growing area, they go openly. They cooperate with the State and local agricultural authorities, and they make every effort to be helpful. Unfortunately, the FDA laboratory facilities are extremely limited and cannot make tests for pesticide residues for all those who would like to have such tests made. However, if any of the samples collected from farms show high residues, the appropriate State authorities are immediately alerted so that steps may be taken to reduce the residues before the crop is shipped. Two examples of such preventive measures and their effectiveness may be cited.

In the fall of 1955, FDA learned that some growers in Texas were planning to use a chlorinated hydrocarbon pesticide on cabbage approximately 2 weeks before harvest. Past experience had indicated that application of this chemical that close to harvest would yield toxic residues. FDA notified its nearest field office, the United States Department of Agriculture, and the manufacturer of the pesticide chemical. The Department of Agriculture telephoned State agricultural officials, and they, in turn, warned the county agents. The manufacturer notified insecticide formulators in the area and asked them to help prevent misuse of the material. An FDA inspector went immediately to the area and warned the growers at a meeting and by television and radio. As a result, the chemical was not used as planned, and the cabbage crop, when harvested, was safe for shipment.

In another case, some growers sprayed their lettuce with a pesticide the residues of which are not permitted on this crop. The rate of application recommended by the State was doubled, and harvesting was started too soon after spraying. FDA found that there were high residues of the chemical on the lettuce as harvested. It notified the State authorities immediately, and the State authorities directed the growers to trim the lettuce severely at harvest to remove the outer leaves containing the poison. One grower shipped two carloads of lettuce without trimming it, and they were seized by the FDA.

FDA would much rather prevent violations than seize crops. Seizure action is reserved for extreme cases. Ordinarily, preventive measures are adequate to insure the shipment of satisfactory produce.

In commenting on seizures, George P. Larrick, Commissioner of Food and Drugs, said: "Growers do not have excessive spray residues on their crops when they observe proper precautions in using agricultural sprays and dusts, but misuse of such chemicals can leave poisonous residues that make a crop illegal in interstate commerce."

State and local health departments will continue to receive reports of injury and illness attributed to pesticide residues in food. In many instances investigation will show that pesticides are not at fault.

However, there may be occasions when misuse of a pesticide will leave dangerous residues on food. In these instances the health department can be of great value to agriculturalists and to the Food and Drug Administration by determining, among other things, what pesticide was employed, when it was applied to the crop, what rate of application was used (generally in pounds of actual pesticide per acre of crop), what stickers, spreaders, or adjuvants were employed with the chemical, when the crop was harvested, and what methods were em-

ployed to reduce the residue, such as washing or brushing or discarding of outside leaves of such crops as cabbage and lettuce. This type of information will help those responsible for recommending spray schedules to determine whether present label directions on pesticides are in need of revision.

An example of the type of misuse that may cause difficulty occurred last year in southern California: To control aphids, a grower sprayed a field of mustard greens with nicotine sulfate solution a few hours before harvest. The nicotine sulfate was old and the grower assumed that it was weak. He prepared a spray twice as strong as recommended. Then, because the aphid infestation was heavy, he applied it at four times the recommended rate per acre. The mustard greens were harvested less than 24 hours after spraying and marketed immediately. State and local health authorities embargoed outstanding lots of the greens when they began causing illness. Samples of the greens contained 70 to 90 parts per million of nicotine.

FDA appreciates reports of this type of misuse. They will help determine how well established tolerances are being met in actual practice. Reports may be sent to the nearest FDA district office or to headquarters in Washington, D. C.

Research in Cancer Chemotherapy

Under contract with the Public Health Service, five laboratories are engaged in large-scale screening of chemical compounds in the search for drugs useful in treating cancer. It is expected that they will test approximately 2,000 compounds by July 1, 1956.

The laboratories, which began work early this spring, are: Microbiological Associates, Bethesda, Md.; Wisconsin Alumni Research Foundation, Madison, Wis.; Southern Research Institute, Birmingham, Ala.; Hazleton Laboratories, Falls Church, Va.; and Stanford Research Institute, Menlo Park, Calif. The Cancer Chemotherapy National Service Center of the Public Health Service National Cancer Institute has the responsibility for supervising the contracts.

Each compound will be tested against three different kinds of mouse tumors implanted into various strains of mice bred for cancer susceptibility, under procedures for animal screening established by a panel of the Cancer Chemotherapy National Committee. This committee, representing the leading organizations and Government agencies in the field of cancer research, was established in May 1955 to sponsor a national voluntary program of cooperative research and development in cancer chemotherapy.

At present, surgery and radiation are the only means of achieving cancer cures, but some forms of cancer, such as acute leukemia, are not amenable to these treatments. Other forms may be diagnosed only after they have spread throughout the body, too late to be benefited by either surgery or radiation. In such cases, chemical treatment appears to offer the greatest hope. Compounds now in use have been successful in prolonging the useful life of patients suffering from cancer of the breast or prostate or cancer of the blood-forming tissues, but these compounds are not curative.

Certification of Coal-Tar Colors

By G. ROBERT CLARK, Ph.D.

Use of toxic dyes in food was one of the public health problems which led to the passage of the original "pure food law" in 1906. Today, 50 years later, protection of the public from dyes that are harmful to health is still an important purpose of the Federal food and drug legislation.

The Federal Food, Drug, and Cosmetic Act of 1938 provides that coal-tar colors used to color any products subject to the act, except hair dyes, must be from batches certified for such use under regulations promulgated by the Secretary of Health, Education, and Welfare. It characterizes food, drugs, and cosmetics containing uncertified coal-tar colors as adulterated. The law applies both to products manufactured in this country and to imports.

The term "coal-tar color" as used for purposes of the law means any coloring matter that is or may theoretically be derived from coal tar. It has continued in the language since the days when coal tar was the only source of many organic chemicals that are now obtained from various sources, particularly petroleum. The word "color" is usually used instead of "dye" because, in the trade, the word "dye" refers only to soluble material; it does not include insoluble material such as that used to color face powder. However, the two words are frequently used without this distinction.

Dr. Clark is chief of the Division of Cosmetics, Food and Drug Administration.

Coal-tar colors are made from a number of chemical compounds called intermediates. If these intermediates have one thing in common, it is their high toxicity. Almost all dye intermediates are known to be poisonous.

Many of the thousands of known coal-tar colors are extremely toxic when taken internally. Some are irritants and sensitizers when applied to the skin. Some are carcinogenic. Actually, comparatively few colors have ever been tested to determine their safety for use in foods, drugs, and cosmetics. Colors need to be so evaluated, of course, only if such use is contemplated.

Dyes, like many other chemicals, are manufactured in reaction vessels from chemical compounds that, in turn, have been manufactured. In these processes, the dye may pick up such materials as lead, arsenic, mercury, cadmium, or chromium. For most uses, these do no harm, but in food, drugs, or cosmetics, they are likely to be a hazard to health.

From this brief description of coal-tar colors, it is obvious that food, drugs, and cosmetics should contain only thoroughly tested colors. The colors themselves must be nonhazardous, and they must be free from harmful quantities of contaminants. The provisions of the Federal Food, Drug, and Cosmetic Act that require certification of coal-tar colors were designed to make certain that only "harmless" dyes are used in products subject to that act.

The color certification program of the Food and Drug Administration is designed to carry out the provisions of the act pertaining to coal-tar colors. This program, which is one func-

tion of the Division of Cosmetics, is set up to do the following:

1. To list colors as certifiable when there is evidence to show that they are harmless and suitable for use, and that practical and accurate methods of analysis are available. New colors are added only on the basis of specific requests by manufacturers.

2. To conduct such analytical and investigative work as may be necessary to certify batches of coal-tar colors. Certificates are issued for individual batches on the basis of analyses of samples submitted by the manufacturer.

3. To conduct enforcement activities to insure compliance with the law.

Fees for certification based on the weight of the batches are paid by the manufacturer. These fees equip and maintain the certification service.

It is the aim of the Food and Drug Administration to achieve the following with respect to coal-tar colors:

1. Each color listed as certifiable must be completely characterized chemically. A sample of each batch manufactured must be completely analyzed chemically to make certain that it does not differ materially from the material submitted to pharmacological testing.

2. Each color listed as certifiable must have been thoroughly evaluated by pharmacological investigation. This investigation must show that the color is harmless and suitable for use.

Almost constant investigations are carried on in the attempt to realize this optimum state of affairs. When new techniques of analysis become available, they are applied to coal-tar colors.

History of Color Certification

Official recognition of the possibility of hazard to health in the use of synthetic dyes in food was evident as early as 1900. The appropriation for the Bureau of Chemistry of the Department of Agriculture, May 25 of that year, included funds "to enable the Secretary of Agriculture to investigate the character of proposed food preservatives and coloring matters, to determine their relation to digestion and health and to establish the principle which should govern their use. . . ." Several Food Inspection Decisions issued under this authority were in respect to foods offered for import into the United States. These decisions required notification of the addition of preservatives and colors to foods and freedom of such additives from deleterious properties.

Certification of colors used in food was begun in 1907, when the Federal Food and Drugs Act of 1906 became effective. Under this act, a list of colors permissible for use in food was adopted by the Board of Food and Drug Inspection, and certification of batches of these colors by the Department of Agriculture was optional with the manufacturer. Use of noncertified colors could not be a basis for regulatory action unless it could be shown that the food might be injurious to health by reason of harmful components of the colors used. It was not until 1939 that certification of batches of colors became mandatory and certification of colors used in drugs and cosmetics was begun.

The rules originally used in selecting colors for food, as stated in 1912 by Dr. Bernard C. Hesse in the Bureau of Chemistry Bulletin No. 147, were as follows:

Rule I: All colors which have not been physiologically tested either on man or animals shall not be permitted for use in foods.

Rule II: All colors which have been examined but with contradictory results shall not be permitted.

Rule III: All examined colors which are doubtful shall not be permitted.

Rule IV: Only those colors on the United States market in 1907 which are of definite composition and which have been examined with favorable results shall be permitted.

The adoption of colors today is based on the same principles. However, the tests applied are much more rigid and extensive than those used in 1907.

Under the original color regulations, certificates for individual batches of colors were issued by the Department of Agriculture on the basis of an affidavit of analysis by the manufacturer and a second affidavit of analysis by a competent scientist. These certificates were not based on analyses made by the Department; rather, they were approvals of the affidavits submitted by the manufacturer. Later actions set up a system of certification of batches based on

analyses made by the staff of the Department. This system made possible standardization of methods, and it is the basic system in use today.

From time to time, additional colors were added to the original list. Two colors, butter yellow (*p*-dimethylamino-azobenzene) and Sudan I (1 phenylazo-2-naphthol), were listed as certifiable and then withdrawn about 6 months later, on June 7, 1919. These colors were removed from the list because they produced a skin rash on persons handling them in quantity. The carcinogenic properties of butter yellow are now well known, but no hint of these properties was disclosed until several years after use of that color in food had been abandoned. In 1938, when the new law was passed, there were 15 colors listed as certifiable, all of which had been listed for at least 9 years.

Regulations Under the 1938 Act

When certification of colors for food, drugs, and cosmetics became compulsory, prompt adoption of lists of suitable colors was essential. After discussions with the dye manufacturers and representatives of the food, drug, and cosmetic industries, a number of colors were selected. They were tested chemically and submitted to such tests for toxicity as facilities permitted. Because it was necessary to adopt lists quickly in order to prevent a chaotic situation in the industries, the tests were considerably less than optimum. The chemical information was sometimes incomplete and sometimes, it was later learned, based on erroneous literature. The pharmacological information suffered from lack of data about the chronic toxicity of the dyes. The final step in the selection of colors was a series of hearings at which any interested party was permitted to testify and to cross-examine witnesses.

Following these hearings, regulations listing certifiable colors were adopted. These are substantially the regulations now in force. The colors are separated into three classes:

FD&C colors: Certifiable for use in coloring food, drugs, and cosmetics. These included all the colors that had been listed under the 1906 act.

D&C colors: Certifiable for use in coloring drugs and cosmetics, but not in food. These colors were all new to certification.

Ext D&C colors: Certifiable for use in coloring externally applied drugs and cosmetics, but not for food or for drugs or cosmetics applied to a mucous membrane. These also were colors not previously certifiable.

No colors are certified for use in the area of the eye, since no drugs or cosmetics intended for use in this area may be colored with any coal-tar color.

Shortly after the first regulations under the 1938 act were adopted, three additional colors were added to the FD&C list. Two of these were oil-soluble dyes, FD&C Orange No. 2 and FD&C Red No. 32, used principally in the external coloring of oranges. The other was FD&C Yellow No. 2, the potassium salt of 2,4-dinitrol-1-naphthol-7-sulfonic acid. (FD&C Yellow No. 1 is the corresponding sodium salt.) Oddly enough, no batch of FD&C Yellow No. 2 has ever been certified.

Later actions added one color to the list of Ext D&C dyes and placed one of the original D&C colors on the FD&C list as FD&C Violet No. 1.

The preparation and adoption of the coal-tar color regulations was a remarkable feat of cooperation between Government and industry. Both parties combined in the effort to make the regulations practical for the industry and effective for protection of the public. It is a tribute to their success that no basic changes in the regulations have been made except those dependent on information not available in 1938.

Recent Activities

It was realized in 1938 that the lack of data about chronic toxicity of coal-tar colors was a matter that required attention. Some studies were conducted, but the imminence of war and the war itself made it impossible properly to attack the problem until several years later.

Research in development of improved methods of chemical analysis was continued, but this work also was largely suspended during the war years. After the war, the availability of new apparatus, particularly spectrophotometric instruments, made progress much more rapid and results more certain.

Certification of FD&C Yellow No. 6

Specifications and procedures for FD&C Yellow No. 6 illustrate the requirements that colors must meet and the tests they must undergo in order to be certified.

General Specifications for All FD&C Colors

"No batch of a straight color listed . . . shall be certified under these regulations unless—

"(*a*) It is free from all impurities (other than those named in paragraph (*b*) or in the specifications set forth . . . for such color) to the extent that such impurities can be avoided by good manufacturing practice.

"(*b*) It conforms to the following specification: (1) In the case of a straight color listed in section 9.3 [i. e., an FD&C color]—

Lead (as Pb), not more than 0.001 percent.

Arsenic (as As_2O_3), not more than 0.00014 percent.

Heavy metals (except Pb and As) (by precipitation as sulfides), not more than trace."

Specific Requirements for FD&C Yellow No. 6

FD&C Yellow No. 6 is described as a "disodium salt of 1-*p*-sulfophenylazo-2-naphthol-6-sulfonic acid." It must meet the following requirements:

Volatile matter (at 135° C.), not more than 10.0 percent.

Water insoluble matter, not more than 0.5 percent.

Ether extracts, not more than 0.2 percent.

Chlorides and sulfates of sodium, not more than 5.0 percent.

Mixed oxides, not more than 1.0 percent.

Subsidiary dyes, not more than 5.0 percent.

Pure dye (as determined by titration with titanium trichloride), not less than 85.0 percent.

Analytical Determinations

Determination of total dye in the sample by titration with titanium trichloride, which quantitatively reduces the azo group.

Determination of the identity and quantity of dye by spectrophotometric procedures. Spectra in the visible, infrared, and ultraviolet regions are obtained and compared with spectra obtained from standard samples prepared in the FDA laboratories.

Determination of sodium chloride, sodium sulfate, insoluble matter, and volatile matter.

Determination of subsidiary dyes. Sodium salts of the following may be present: 1-phenylazo-2-naphthol-6-sulfonic acid, present if the sulfanilic acid used as an intermediate contains any aniline; 1-*p*-sulfophenylazo-2-naphthol-3,6-disulfonic acid and 1-*p*-sulfophenylazo-2-naphthol-6,8-disulfonic acid, present to some extent in all samples since it is almost impossible to prepare 2-naphthol-6-sulfonic acid entirely free from the disulfonated compounds; 1-(4 sulfophenylazo)-2-naphthol, present because some betanaphthol may be present in the sulfonated compound.

Determination of ether extracts, a measure of any organic tars or other ether soluble substances that may remain in the intermediates.

Determination of uncombined intermediates, present because of incomplete diazotization or coupling. Sulfanilic acid and 2-naphthol-6-sulfonic acid are the intermediates used for FD&C Yellow No. 6.

Determination of mixed oxides (iron, aluminum, etc.) that may be present. These usually get into the product because the processing equipment is attacked by reagents used in preparation of the dye.

Determination of lead and arsenic, usually present in the acids used in the sulfonation and nitration reactions carried out in the preparation of the intermediates.

Determination of heavy metals—copper, bismuth, tin, antimony, cadmium, and mercury. These also get into the dyes from processing equipment.

In addition, to meet the "good manufacturing practice" requirement in the general specifications, it must not contain more than traces of uncombined intermediates or of phenylazo-2-naphthol-6-sulfonic acid. Experience of many years has shown that it is practical to obtain almost complete removal of these impurities.

Certification or Rejection

If the sample is found to meet all the specifications, including the "good manufacturing practice" requirements, a certificate covering the batch is issued. If the sample fails to meet any one of the specifications, the batch is rejected.

Recent chemical investigations have shown that some of the colors do not have the exact composition or structure ascribed by earlier work. This information will probably not affect the status of the colors as certifiable, but it is of fundamental importance in establishing methods of analysis and standards that batches of the colors must meet in order to be certified.

Methods of analysis for coal-tar colors are a part of the program of the Association of Official Agricultural Chemists, and the results of the FDA's chemical investigations are usually published in the journal of that association. A mimeographed publication containing the methods of analysis used in the color-certification laboratory is also available.

Some of the recent pharmacological investigations have produced surprising results. Three colors, FD&C Orange No. 1, FD&C Red No. 32, and FD&C Orange No. 2, have been found to be considerably more toxic than was disclosed by earlier tests. These dyes act as gastrointestinal irritants. The toxicity of FD&C Orange No. 1 and of FD&C Red No. 32 has been confirmed by illness following ingestion of candy or popcorn containing these colors. In each case, the products contained very much more color than is customarily used.

As a result of the new tests, the Secretary of Health, Education, and Welfare issued a regulation removing the three colors from the lists of colors certifiable for use in food and drugs in November 1955. This regulation is now in effect with the exception of its application to FD&C Red No. 32 for coloring the outer skin of oranges. A stay issued by the Fifth Circuit Court of Appeals requires the continued certification of sufficient color for that use until the court has finally disposed of a petition to review the entire regulation. The colors were retained as certifiable for use in externally applied preparations since evidence is available to show that they are safe for such use.

Legal action against excessive use of certified colors is not authorized under the Federal Food, Drug, and Cosmetic Act. Section 406 (*b*) reads: "The Secretary shall promulgate regulations providing for the listing of coal-tar colors which are harmless and suitable for use in food, and for the certification of batches of such colors with or without harmless diluents." Sections 504 and 604 have almost identical wording with respect to colors for drugs and cosmetics.

The meaning of the word "harmless" is the cause of difficulty. The Food and Drug Administration believes the word to mean that the colors must be harmless per se, that is, without regard to the amounts of colors that would or could be consumed by the individual. This means, of course, that the colors must be without detectable physiological effect except that of inert or nonnutritive substances. The absolute harmlessness of any substance is virtually impossible to demonstrate.

The production of certified colors has increased steadily with the general expansion of the national economy. In 1941, about 2¼ million pounds of coal-tar colors were certified in 3,677 batches. In 1955, the amount was more than 5 million pounds in 4,675 batches. These figures include not only the highly concentrated "straight" colors, but also mixtures of the colors with various diluents, such as salt, sugar, or water. Such mixtures, which may contain two or more colors as well as diluents, are usually used instead of the straight colors in coloring food.

Certification of the 4,675 batches of coal-tar colors in 1955 required more than 25,000 analytical determinations, or about 100 per working day. An example of the certification requirements and procedures is given on page 584.

There have been very few regulatory actions against products containing uncertified colors in recent years. The requirements of the law are well known, and the food, drug, and cosmetic manufacturers generally make every effort to comply. In a few instances, products made in other countries have been denied entry into this country because they were found to contain uncertified colors.

Investigation of the production procedures used by the manufacturers of straight colors and mixtures has shown that few have failed to follow the regulations in every particular.

Program Needs

By law, the listing and certification of coal-tar colors is performed only upon payment of such fees as may be necessary to provide, main-

tain, and equip an adequate service for such purposes. Hence, the certification program is not handicapped by a lack of funds. But as demands for services increase, it is necessary to adjust facilities and personnel accordingly. Since the present program is the maximum that can be contained in the available laboratory and office space, relocation of the facilities is a matter for immediate attention. Recruiting and holding an adequate supply of personnel is a chronic problem, but at the moment at least all assigned positions are filled.

Drugs and Medical Devices

By ALBERT H. HOLLAND, Jr., M.D.

The medical program of the Food and Drug Administration is concerned primarily with assuring the safety of drugs and medical devices to protect public health as provided by law. Secondarily, it advises the Commissioner's Office and the other scientific and administrative programs of FDA on medical matters.

The major elements of the medical program may be characterized by the words "Stop, look, and listen." As provided by law and regulation, FDA attempts to stop the violator; it looks at new drug applications and medical investigative data; and it listens to what is going on generally in the drug and device industries so that proper preventive or remedial action can be instituted when necessary.

The objective of the Federal Food, Drug, and Cosmetic Act with respect to drugs is to assure the safety, quality, purity, and identity of all drug products in interstate commerce, thereby fulfilling the ultimate objective of protecting the public health. Drugs imported into this country are subject to the same scrutiny and legal requirements.

Dr. Holland is medical director of the Food and Drug Administration. When appointed to this position in 1954, he was medical director of the Armour Laboratories. He has also served as director of the Office of Research and Medicine, Oak Ridge Operations of the Atomic Energy Commission, and as medical officer assigned to the Manhattan Engineering District project at Oak Ridge.

Actually, all aspects of the medical program are geared to one key word—safety. Purity, quality, identity, and labeling, including therapeutic claims, must all measure up to the requirements imposed by the reasonable application of the concept of safety.

It is perhaps of significance that the original Federal food and drug legislation, the Food and Drugs Act of 1906, was conceived and enacted by the Congress at the behest of a physician, Dr. Harvey W. Wiley, who was at the time chief chemist of the Department of Agriculture. The Food and Drug Administration, therefore, has a medical heritage of which it can well be proud and which clearly establishes it, both historically and for the future, as a public health agency of government.

Responsibilities and Functions

The New Drug Branch of the Division of Medicine bears the responsibility for reviewing new drug applications in detail, interpreting the investigative data, and permitting or denying the introduction of a new drug into interstate commerce. Its task is one that requires the exercise of the highest degree of good judgment and medical acumen. It is one thing to assess the investigative results obtained by a few medical experts in carefully selected patients under controlled conditions; it is quite another to extrapolate that data to nationwide use—perhaps indiscriminate use by some physicians or by the public if the drug is one that may legally be sold without a prescription.

The Veterinary Medical Branch has the same purview of new drugs for animal use as does

the New Drug Branch of drugs for human use. In addition, it has a regulatory or enforcement function for all veterinary medicinals, be they old or new drugs.

The Drug and Device Branch works primarily to obtain compliance with, and enforcement of, the law with respect to the safety and adequacy of labeling of drugs and medical devices in interstate commerce. But to apply scientific judgment in a court of law entails peculiar difficulties. Medicine at its best is still far from being an exact science. Biological variation and biological response in the subject, as well as variations of interpretation by the investigator, frequently preclude satisfactory quantitation. The art and the science are not always clearly distinguishable, and opinion and fact are not always readily separable. That this is true becomes evident when FDA resorts to legal measures to achieve enforcement and control. Honest admission of uncertainty by a scientific witness may too often strike a jury as "reasonable doubt" as to the guilt of the defendant. To reach a bona fide medical conclusion is one thing; to prove it beyond reasonable doubt in a court of law is quite another.

One important aspect of assuring the safety of drugs and devices is preventing misbranding. The legal definition of misbranding has many facets. Those readers who are responsible for enforcing parallel State laws know them well; for others, a few basic concepts that illustrate the philosophy of the law may be mentioned here.

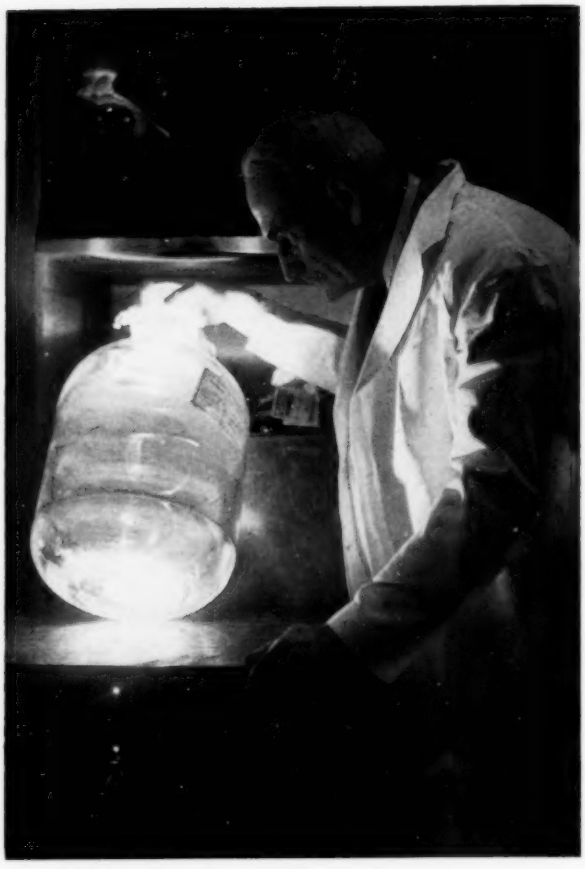
A drug or device is deemed to be misbranded:

1. If its labeling is false or misleading in any particular.

2. If, in finished or bulk package form, it fails to bear a label giving the name and place of business of the manufacturer, packer, or distributor, and an accurate statement of contents.

3. If any word, statement, or other information required under the authority of the act to appear on the label or labeling is not displayed with such conspicuousness and in such terms as to make it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

4. Unless its labeling bears adequate directions for use, adequate warnings against use in pathological conditions or by children when such use may be dangerous to health, and adequate warnings against unsafe dosage or methods or duration of administration or application. This does not, however, apply to household chemicals except those specifically covered in the Federal Caustic Poison Act. Under the Federal Food, Drug, and Cosmetic Act all drugs are subject to this requirement.



FDA inspector in the stock room of a drug factory producing injectables. The bulk solutions are examined for undissolved particles before they are packed and sealed in ampules.

From the foregoing it is apparent that the food and drug legislation is designed to inform and protect the user of drugs or devices whether he be a physician or a patient. While the law is designed to protect, it is well also to recognize its limitations. The Federal Food, Drug, and Cosmetic Act applies only to the content and labeling of products shipped in interstate commerce. The Food and Drug Ad-

ministration, therefore, is not responsible for advertising, which is regulated by the Federal Trade Commission. FDA does, however, cooperate with the Federal Trade Commission, usually by making, at its request, laboratory studies of products in question. In addition, FDA provides the medical support for fraud cases brought by the Post Office Department.

Techniques of Control

To carry out the provisions of the law, the Food and Drug Administration employs many techniques. It maintains a nationwide inspection staff of approximately 250 men who devote their time to food and drug inspections in all channels of distribution from manufacturer to the ultimate distributor. It also maintains a series of field laboratories where samples of drugs are analyzed.

FDA is in continuing contact with all segments of the drug trade and with the medical profession. It is now in the process of enlarging its file of reports on injuries from drugs and household chemicals. The Research and Reference Branch of the Division of Medicine is interested in all types of drug injuries or suspected injuries whether they culminate in death, blood dyscrasias, sensitivity reactions, or other toxic manifestations. Often it is only by slowly and painfully piecing together the puzzle that a significant pattern is found. FDA must and does maintain constant surveillance of the medical literature and medical reports, as well as its incoming mail. Recently, the medical staff has had occasion to work with those interested in the operation of poison control centers throughout the country.

Public health officials can be of great assistance to the Food and Drug Administration in providing the protection which the law intends and which so many people take for granted. For example, health officers often are in a position to supply information about the business of a cancer quack, about medical devices which may not meet the requirements of the law, or about injuries caused by drugs.

About a cancer quack, FDA needs to know such things as how he is operating his racket, the names of his patients, when his patients die, and findings of autopsies.

About medical devices, FDA needs to know: When and where are they sold and used and by whom? What claims are made for them? Is an interstate shipment involved? Is there label copy or descriptive literature available?

An immediate report of a drug injury or a suspected injury containing all the facts available is of utmost importance. What was the drug used? How was it administered? By whom? What dosage was employed? What is the name of the manufacturer? of the patient? of the physician? Too frequently FDA does not hear of adverse experiences with drugs until months after they occur, when the details crucial to intelligent interpretation have been forgotten or are no longer available.

To protect the public against adulterated or misbranded medicines, as provided by law, the Food and Drug Administration needs the assistance of all persons who are concerned with health, whether they be physicians in private practice, officials of government agencies, or members of the drug and device industries. It also needs the understanding and cooperation of an informed public.

Assuring the Safety of New Drugs

By RALPH G. SMITH, M.D.

Before the Federal Food, Drug, and Cosmetic Act was passed in 1938, new drugs could be introduced into interstate commerce without approval from any Federal agency or without consultation with any Federal agency. The distributor had no responsibility under Federal law for the safety of the new product. The marketing of drugs was subject to the provisions of the Food and Drugs Act of 1906, which dealt with adulteration and misbranding of drugs only after a drug was in the channels of distribution. The 1906 act did not deal directly with safety of drugs.

Although many of the drugs on the market in 1938 were satisfactory, further control was needed. With the advancement of pharmaceutical chemistry and the expansion of pharmacological research and screening procedures, particularly by industry, many new products were becoming available for drug use.

Most of the new products were synthetic compounds, but a few were purified active agents of old galenical drugs or derivatives of these agents. Many had specific pharmacological actions and were, accordingly, of interest from the therapeutic standpoint. In addition to useful therapeutic actions, however, some of the new products possessed potentialities for harmful effects. As with all new compounds, the nature of these effects and the margin of safety could be revealed only by appropriate study. Some control, additional to the judgment of the distributor, on the safety of the drug seemed to be in the public interest.

Accordingly, early drafts of the Federal Food, Drug, and Cosmetic Act included a provision that a drug was misbranded if it was unsafe for the use suggested in its labeling. By a coincidence, the well-known elixir of sulfanilamide disaster, which occurred while the bill was under consideration, convinced the Congress of the necessity for new drug provisions in the law. As a result of a new toxic vehicle or solvent in the sulfanilamide product, more than 100 deaths occurred within a very short time and before adequate warnings or removal of the drug from the market was possible.

Dr. Smith is chief, New Drug Branch, Division of Medicine, Food and Drug Administration.

For Effective Application

The new drug section of the 1938 act prohibits the distribution in interstate commerce of a new drug until an application for it is effective. In order for the application to become effective, adequate evidence that the drug is safe when used according to the labeling furnished for it must be included in the application.

Applications for new drugs are received and reviewed by the New Drug Branch of the Division of Medicine, Food and Drug Administration. The review procedure calls for the assistance of other FDA technical divisions whenever indicated. The advice of original investigators or of other organizations or of experts outside the FDA may be sought in specific instances.

Since products which are not new drugs may still be introduced into interstate commerce without any legal formalities or even notification to the Food and Drug Administration, it is of obvious importance to decide whether a drug is new. In many instances the answer is apparent, but in certain cases some definite criterion is necessary for a decision.

A definition of a new drug is included in the 1938 act. In simple terms, a new drug is a drug which is not generally recognized, by experts qualified to evaluate the safety of drugs, as safe when used as directed in its labeling.

A yardstick is even more necessary to determine when a product ceases to have the status of a new drug. This point is also covered by definition in the act. Even though sufficient evidence may be available from investigative studies to show that a drug is safe for use, the drug continues to be considered as a new drug until it has been used to a material extent or for a material time under the conditions set forth in its labeling.

Continuance of a product in new drug status for a considerable period of time is significant in two ways. It means that the product must not only be indicated as safe by investigative studies but that it must stand the test of use under ordinary marketing conditions before it loses its new drug status and is freed from the restrictions which the status entails. It also means that any company wishing to market the drug must also obtain an effective new drug application even though the drug is already being distributed by the company holding the original effective application. Each additional application must include adequate evidence of the drug's safety.

The definition of a new drug is further interpreted by regulation. Food and drug regulations point out that a product may be considered new not only when it contains a new active ingredient but also when it includes a new excipient, coating, menstruum, carrier, or other component. A new combination of two or more old drugs or a change in the usual proportions of the ingredients in an old combination may cause the product to be considered a new drug. A new use, a new dosage schedule, or a new route of administration for a commonly recognized drug may also result in a new drug within the meaning of the definition.

In many instances little difficulty arises in deciding that a drug is new, but there are also numerous cases in which a decision can be reached only by careful consideration of all available facts. It must be determined whether the changes from recognized formulations or therapeutic procedures are sufficiently significant to raise a question of safety. An honest difference of opinion on the new drug status of a product occasionally arises between the manufacturer and the Food and Drug Administration. The difference may be resolved in either direction on consultation. Generally, however, the advice of the Food and Drug Administration is accepted although the Federal courts have the jurisdiction for deciding the matter.

Although the new drug section of the 1938 act is applicable to most new drugs, there are certain exemptions. Drugs which were distributed under essentially the same labeling prior to the effective date of the act (June 25, 1938) are excluded by definition even though they may not be generally recognized as safe. Vaccines, serums, toxins, antitoxins, and most blood products which are licensed under the Biologics Control Law enforced by the Public Health Service are exempt by regulation from the new drug procedure. Likewise, the five antibiotics, penicillin, streptomycin, aureomycin, chloramphenicol, and bacitracin, and derivatives of those antibiotics that are subject to certification by the Food and Drug Administration are exempt by law from the new drug section of the act.

For Safe Use of a Drug

The application should contain detailed reports of well-planned animal and clinical experiments. Data of the following type are important: the age, sex, and pathological condition of the subject; the dose of the drug used; the frequency and duration of administration; the results of clinical and laboratory examinations; the nature and incidence of adverse effects; and the therapeutic results.

Animal studies are usually considered necessary, particularly if the product contains an ingredient new to therapeutics. These studies demonstrate the nature of the pharmacological action of the drugs and also the type of effect

obtained by overdosage. Acute toxicity experiments yield a measure of the therapeutic index or safety margin. Subacute and chronic experiments with hematological examinations and histopathological studies give additional information in this connection. The clinical investigator may be expected to demand reports of such studies before he uses the drug on patients.

The type of investigation, both animal and clinical, should be determined by the proposed use of the drug with respect to method and duration of administration. A drug which is recommended for the treatment of chronic conditions such as arthritis, epilepsy, or parkinsonism will require animal toxicity studies of prolonged duration. Shorter toxicity studies would suffice for a drug such as a general anesthetic for use in a single administration. Likewise, a chemotherapeutic agent indicated for the treatment of an acute infection would be used only for a few days to a week or so and, consequently, would not require prolonged animal toxicity studies. Drugs for topical application, such as ointments, lotions, and topical anesthetics and antiseptics, should include studies on their potentiality to produce primary irritation and sensitization. Information on the degree of absorption from skin or mucous membranes may also be indicated when there is a question of systemic toxicity.

The application must also include a full list of the components which go into the preparation of the drug even if they do not appear in the final product. Their disclosure is of interest from the standpoint of their possible retention as impurities in the finished preparation. A complete quantitative statement of the composition of the drug is an obvious requirement. A description of the manufacturing methods and control procedures used in producing the new drug is required to provide the assurance that a preparation of definite specifications with respect to identity, strength, quality, and purity will be produced.

A sample of the drug may be required with the application, and completed market packages are required as they become available. Finally, copies of the proposed labeling must be furnished as part of the application since the safety of the drug must be evaluated on the basis of all the conditions under which it is recommended for use.

If the New Drug Branch is satisfied that the drug will be safe when used as proposed, the application is allowed to become effective, which means that permission is granted for distribution of the new drug in interstate commerce.

Marketing New Drugs

Since a drug retains its new drug status for some time after initial distribution, its use under actual marketing conditions is a further test of safety and usually a more severe test than the carefully supervised investigative studies. The general distribution of a drug which appears safe on the basis of investigative studies may be followed by reports of effects of an unexpected nature or of a higher incidence of side effects than occurred in preliminary use. Provision is made in the law to suspend an effective application under these conditions if the hazards of use are considered sufficiently serious. Applications have been suspended for this reason.

Much experience has been gained in the new drug section in the 18 years since the act was passed. As of January 31, 1956, applications for new drugs numbered 10,350, and 7,365 became effective. These figures include applications for veterinary medicaments, which account for approximately 18 percent of the applications submitted since July 1, 1954.

The 3,000 applications which did not become effective fall largely into three classes. Approximately 1,800 were incomplete. Some 500 were withdrawn, usually as a result of objections based on inadequate showing of safety. About 600 were not considered to be new drugs and, accordingly, did not require an effective application for marketing. Action is still pending on 100 applications.

The fact that 7,365 applications became effective does not mean that 7,365 new chemical compounds were introduced as therapeutic agents during the 18-year period.

Numerous firms may submit an application for the same drug. Separate applications may be submitted for various dosage forms of the same drug, such as oral preparations and injections. Or, the new drug in combination with a variety of old drugs may account for a num-

ber of applications. Although each application does not represent an entirely new chemical substance, it does represent a distinct effort by both the manufacturer and the Food and Drug Administration to assure that the consumer can use the product with safety.

The distributor, in addition to following the marketing experience of the new drug, frequently has occasion to change the provisions of his effective application. He may find it advisable to modify certain procedures in the manufacturing process, to make changes in the formulation, or to revise the labeling. A revision of the labeling may involve the inclusion of a warning statement or an additional indication for use of the drug, or it may provide for the product to be distributed under the label of another company.

Changes in the effective application may be made by submitting supplements, which are processed in the same manner as the original application. This procedure is in effect as long as the product remains a new drug. In view of the large number of effective applications on file, it is not surprising that the current number of supplementary applications and related correspondence exceeds 4,500 pieces a year.

It is probable that the safety of the new drug would be achieved in most instances without governmental control. The control procedure, however, is justified if it prevents even rare instances of injury by the distribution of drugs. The necessity of additional safeguards was felt in 1938 when the new drug section of the act was introduced. Since that time, the necessity has become still more imperative because of an even more rapid increase in the production of new products with a potentiality for drug use.

The Calculated Risk

The New Drug Branch has seen the quality of new drug applications improve during the past few years. A concept of adequate investigation of a new drug has been gradually developed by the Food and Drug Administration and by the pharmaceutical companies so that today new drugs are being investigated more thoroughly than ever before. Greater precautions are being taken by the adoption of stricter manufacturing control procedures to assure the marketing of products of specified potency and adequate purity. The new drug procedure has been instrumental in promoting these achievements.

Such safeguards should justify the physician's reliance on the declared potency and purity of the product he administers or prescribes and should strengthen the patient's trust in the safety of the remedy. In spite of this, certain facts should be kept in mind.

Safety is a relative term. Probably no two drugs are safe to the same degree. The wide variation in individual tolerance to drugs is recognized. Consequently, a wide margin between the effective dose and the toxic dose is essential if the drug is to be safe for the vast majority of potential consumers. The wide margin of safety is particularly necessary for remedies which are not life saving or which are used for conditions amenable to treatment by other methods or drugs that are relatively safe. In contrast, applications may be allowed to become effective for drugs that are known to be dangerous and for which the safety margin is critical. Granting of these applications is considered to be justified only when the drugs are useful as a life-saving or life-prolonging measure in conditions for which there is no safer efficacious remedy.

In the use of drugs which involve a calculated risk, their potentialities for harm are decreased if the physician recognizes that the potentialities exist and takes all possible precautions against adverse occurrences. Usually, care is taken in the labeling of a drug to outline optimal dosage ranges from the standpoint of both efficacy and safety and to include necessary warnings, precautions, and contraindications for its use. Careful labeling can serve its purpose only if it is read. With the introduction of so many new drugs, the physician can become familiar with only a few. Those which he selects, however, should be studied with particular care by taking advantage of all information imparted in the labeling instructions and in the published literature. The physician can contribute significantly to the safety of a new drug by reporting to the Food and Drug Administration, or by publication, any adverse reactions he observes in his practice.

Certification of Antibiotics

By HENRY WELCH, Ph.D.

It is generally agreed that little if any good is accomplished by wars. Penicillin perhaps is the exception, for its development, rapid availability, and wide use stemmed from the great need for the drug in World War II. Similarly, the antibiotics certification program got its initial impetus because of our entrance into this worldwide conflict.

In 1941 there was insufficient penicillin in the United States to treat a single case, and in 1942 probably not enough to treat a hundred cases. However, by September 1943 there was sufficient penicillin to satisfy the early demands of the Armed Forces of this country and those of our allies.

It was during September 1943, at the request of the Armed Forces and the War Production Board of the United States, that the Food and Drug Administration undertook the testing of each lot of penicillin produced, for potency, sterility, toxicity, pyrogenicity, pH, and moisture content. On the basis of the results obtained by these tests, the lot was either accepted or rejected.

By June 1945 there was sufficient penicillin to satisfy not only the Armed Forces but a great civilian demand as well, and there was an apparent need for a method of control for this important therapeutic agent. On July 6, 1945, the Federal Food, Drug, and Cosmetic Act was amended to require the certification of batches of drugs composed wholly or partly of any kind of penicillin. The Federal Security Administrator, in accordance with the provisions of this amendment, promulgated regulations providing such standards of identity, strength, quality, and purity as would insure the safety and efficacy of penicillin and penicillin preparations.

Under the law, each manufacturer, before distributing a batch of penicillin in interstate commerce, must submit samples of the batch to the Food and Drug Administration for examination and must obtain a certificate showing that it complies with applicable regulations. Each product proposed for certification to the Food and Drug Administration must be shown to be safe and efficacious, this proof being based on actual clinical trial.

In 1947 the Federal Food, Drug, and Cosmetic Act was amended to include streptomycin and its derivatives. In 1949 it was further amended to include aureomycin (chlortetracycline), chloramphenicol (chloromycetin), and bacitracin. Tetracycline, being a derivative of aureomycin, is also certified by the Government.

There have been no amendments to the act since 1949 to require the certification of antibiotics developed since that time. Therefore, all other currently available antibiotics are subject only to the general provisions of the act, unless they are added to one of the antibiotics for which certification is required.

Growth of the Antibiotics Industry

When penicillin was first produced in the United States, the potency and hence the purity

Dr. Welch is director of the Division of Antibiotics, Food and Drug Administration. Since its beginning in 1943, he has been in charge of the FDA's antibiotics certification program. He is a co-author of the books, Antibiotic Therapy (1951) and Principles and Practices of Antibiotic Therapy (1954); the editor of the Manual of Antibiotics (1954); and the editor in chief of the journals, "Antibiotics and Chemotherapy" and "Antibiotic Medicine."

was quite low. Early assays of this drug indicated average potency ranges from 100 to 200 units per milligram. The purity of penicillin improved rapidly in the first few years of manufacture, and the crude material, consisting of a dark brown, amorphous powder, gradually changed in color and consistency to a light brown, then yellow, and finally, the white crystalline form. Production amounted to only about 29 pounds in 1943.

When penicillin became available for the civilian population in 1945, the purity of the drug had been improved considerably so that the calcium salt, which was the one used to the greatest extent, had a potency on the order of 1,200 units per milligram. The crystalline drug (sodium penicillin), which soon appeared, had a potency of 1,667 units per milligram.

During the war years and for some time thereafter, 20 manufacturers in this country produced practically the entire world's supply of penicillin. Competition as such did not exist. All that was produced was consumed and the price was high. The Army paid as much as $20 for each 100,000 units. By contrast, in late 1955 the Army purchased penicillin in vials packed in wooden cases for shipment overseas for 5 cents for each 300,000 units; that is, less than 2 cents per 100,000 units. Competition now is extremely keen, and instead of 20 manufacturers of penicillin, there are only 9. In fact, 4 of these 9 account for some 70 percent of the production. In addition to the 9 manufacturers of penicillin, there are 4 others producing antibiotics. These 13 manufacturers are responsible for the great bulk of the world's supply of these important drugs.

Production of penicillin in this country started an industry that today has a capital worth of about $1 billion. In less than 15 years a number of other antibiotic drugs have found their way into the therapy of infectious diseases. In table 1 are the 24 antibiotics that have been shown to be clinically useful of the 3,000 to 4,000 that have been described in the literature. In addition to these 24, hundreds of others are awaiting tests on the shelves of those manufacturers still in the antibiotics field.

Changes in production and approximate dollar value of the seven antibiotics that are

Table 1. Clinically useful antibiotics

Antibiotic	Year developed
Penicillin	1929–1943
Tyrothricin	1939
Streptomycin	1943
Bacitracin	1945
Chloramphenicol	1947
Polymyxin	1947
Dihydrostreptomycin	1948
Chlortetracycline	1948
Neomycin	1949
Fumagillin	1950
Oxytetracycline	1950
Viomycin	1950
Nystatin	1951
Erythromycin	1952
Carbomycin	1952
Tetracycline	1953
Anisomycin [1]	1954
Cycloserine [1]	1955
Cathomycin [2]	1955
Streptonivicin [2]	1955
PA 105 [1]	1955
Vancomycin [1]	1955
Stylomycin [1]	1955
Spiramycin [1]	1955

[1] Still under clinical study.
[2] Although isolated from different sources, cathomycin and streptonivicin have been shown to be the same antibiotic.

used to the greatest extent—penicillin, streptomycin, dihydrostreptomycin, and the broad-spectrum antibiotics—are shown in table 2. Only 29 pounds of crude penicillin were produced in 1943, and this amount had a value at the manufacturers' level of about $3 million. Production increased more than 100 times in 1944. In 1945 the original estimate of 5,000 kg., which was expected to be sufficient to supply the world demand, was exceeded by a considerable amount: Fourteen thousand pounds, or more than 6,000 kg., were produced. Competition in the industry became extremely keen from 1951 on, and although 756,000 pounds were produced in 1953, the dollar value was less than half that of the 636,000 pounds produced in 1951.

The history of the production of streptomycin is not markedly different. The experience in production methods obtained with penicillin resulted in some 3,800 pounds being produced in 1946, the first year that streptomycin was available commercially. This drug, too, when first used was expensive, in the neighborhood of $15 per gram. The competition in penicillin was re-

flected in the price of streptomycin by 1953, and although 375,000 pounds were produced, 100 times as much as in 1946, the value increased only 3 times.

More than 417,000 pounds of the broad-spectrum drugs were produced in 1953, with an approximate value of $137 million. In 1954, 440,000 pounds valued at $150 million were made available.

The broad-spectrum antibiotics and penicillin have uses other than in the prophylaxis and treatment of disease. They are used, for example, in the promotion of animal growth, and in 1954 some 490,000 pounds were produced for feed supplements. The total for all antibiotics in 1954 was some 2,284,000 pounds, with an approximate value at the manufacturers' level of more than $272 million. According to recent estimates, production was not materially different in 1955.

A large number of antibiotic preparations are now available to the physician in this country. Among those preparations sold in greatest quantity, there are more than 300 available for clinical use. Preparations containing penicillin number 150. There are 38 streptomycin and dihydrostreptomycin preparations, 47 chlortetracycline and tetracycline preparations, 25 oxytetracycline preparations, 15 chloramphenicol preparations, and 27 bacitracin preparations.

Table 2. Antibiotic production in the United States, 1943–55

Year	Antibiotic	Pounds	Approximate value in millions of dollars
1943	Penicillin	29	3
1944	do	3, 200	
1945	do	14, 000	
1951	do	636, 000	137
1953	do	756, 000	58
1954	do	860, 000	63
1946	Streptomycin	3, 800	11
1953	Streptomycin and dihydrostreptomycin.	375, 200	35
1954	do	494, 000	40
1953	Broad-spectrum [1]	417, 600	137
1954	do	440, 000	150
1954	Feed supplements [2]	490, 000	19
1954	All antibiotics	[3] 2, 284, 000	[3] 272
1955	do	[3] 2, 400, 000	

[1] Chlortetracycline, oxytetracycline, tetracycline, and chloramphenicol.
[2] The broad-spectrum antibiotics and penicillin.
[3] Estimated.

Certification Practices and Principles

At the start of penicillin control in 1943, a group of six technicians of the Food and Drug Administration, in collaboration with other governmental agencies, successfully checked for the Armed Forces all penicillin then produced. The apparatus used was hand built and makeshift to meet the requirements of a group of new methods.

As time went on and new antibiotics came into clinical use, the laboratory force was expanded. New and adequate equipment became available, and by 1950 the staff controlling certifiable antibiotics numbered 80. Instead of milligrams of penicillin worth more than its weight in gold, lots containing hundreds of thousands of vials of penicillin were being assayed, and the glass used for packaging cost more than the drug. Assays were performed on a mass scale with automatic equipment (fig. 1), and special reading devices sped up potency determinations and made them more accurate (fig. 2). Electronic equipment for infrared analysis (fig. 3) and for accurate, automatic temperature determinations (fig. 4) simplified considerably the problems of mass assays.

Since its beginning in 1945, the certification program has been self-sustaining. All equipment is purchased from fees paid by the producers of the certifiable antibiotics. In addition, since it is set up on a cost basis, excess fees are returned quarterly to the manufacturers on a pro rata basis.

Under the certification system a producer of a new antibiotic preparation for which certification is required presents to the Food and Drug Administration clinical data demonstrating the safety and efficacy of his proposed product. If the data are found to be satisfactory, a monograph is prepared establishing standards of identity, strength, quality, and purity. Thereafter, samples of each batch produced are forwarded to the Division of Antibiotics for examination, and a certificate is issued on all batches complying with the standards. At the present time some 20,000 batches of antibiotics and their preparations are examined and certified yearly.

Antibiotic preparations destined for export are not required to be certified under the certification system. Such preparations are exempt under section 801 (*d*) of the Federal Food, Drug, and Cosmetic Act, provided they meet the specifications of the foreign buyer, are not in violation of the laws of the country to which they are to be shipped, and are marked clearly for export. The buyer of the foreign country must require that the certifiable drugs pur-

Figure 1. Preparing agar plates for penicillin assays.

Figure 2. Measuring zones of inhibition to determine potency of antibiotics.

Figure 3. Electronic equipment used for infrared analysis of antibiotics.

chased meet United States Government standards if he wishes to obtain certified material. If he does this, the preparations for export must be sampled, tested, and certified before shipment. Consequently, some of the United States producers certify all of their preparations whether destined for the domestic or export market.

Since July 1945, nearly 300 companies have used the certification services. During this period of approximately 10 years, 150,000 batches of various preparations of penicillin, streptomycin, dihydrostreptomycin, chlortetracycline, tetracycline, chloramphenicol, and bacitracin have been examined. Taking the usual daily dose of these drugs to be 300,000 units for penicillin, 60,000 units for bacitracin, and 1 gram each for streptomycin, dihydrostreptomycin, chlortetracycline, chloramphenicol, and tetracycline, the quantity of these drugs examined represents approximately 7 billion daily doses. The average cost paid by the producers for certification of each daily dose was 7/100 of a cent. Over 1,000 batches have been either rejected by FDA or withdrawn by the producer because they were substandard. These substandard batches which were prevented from reaching the consumer represent more than 70 million daily doses.

During the past 5 years, the Administrator of the Federal Security Agency, and later the Secretary of the Department of Health, Education, and Welfare, has found that certification of the antibiotic preparations in the list on page 599 is not necessary to insure safety and efficacy. These preparations are now exempt from certification.

The Impact of Antibiotics

Through use of antibiotics the spectrum of amenable diseases has widened almost yearly. Either completely or partially controlled by the seven antibiotics previously mentioned are

Figure 4. Electronic equipment for automatically determining rectal temperatures of rabbits.

Antibiotic Preparations Now Exempt From Certification

Crystalline penicillin G sodium.
Crystalline penicillin G potassium.
Antibiotics for diagnostic use.
Antibiotics for fish diseases.
Antibiotics as preservatives for bull semen.
Antibiotics as preservatives for biological drugs.
Antibiotics for use as ingredients of animal feed for certain prescribed conditions.
Animal feed mixes intended for certain prescribed conditions.
Buffered crystalline penicillin G sodium.
Buffered crystalline penicillin G potassium.
Certain formulations of penicillin troches.
Certain formulations of bacitracin ointment.
Streptomycin sulfate granules (powder), oral veterinary.
Crude chlortetracycline, oral veterinary.
Antibiotics for agricultural use.
Buffered penicillin powder, oral veterinary.
Penicillin-streptomycin (penicillin-dihydrostreptomycin) tablets, oral veterinary.
Penicillin-streptomycin (penicillin-dihydrostreptomycin) powder, oral veterinary.
Streptomycin (dihydrostreptomycin) for inhalation therapy, veterinary.
Streptomycin hydrochloride (sulfate) solution, oral veterinary.
Chlortetracycline (chlortetracycline hydrochloride) powder, veterinary; tetracycline (tetracycline hydrochloride) powder, veterinary.
Soluble bacitracin methylene disalicylate, oral veterinary.
Bacitracin powder, oral veterinary.

pneumonococcal and streptococcal infections, meningococcal and gonococcal infections, staphylococcal infections, syphilis, yaws, pinta, bejel, Weil's disease, relapsing fever, tropical ulcer, Vincent's angina, and many surgical, urinary, and intestinal tract infections; amebiasis, brucellosis, plague, tularemia, and tuberculosis; and diseases due to certain large viruses and rickettsiae, including primary atypical pneumonia, psittacosis, lymphogranuloma venereum, trachoma, Rocky Mountain spotted fever, epidemic and endemic typhus, scrub typhus, and Q fever. Also largely under control are granuloma inguinale, chancroid, Carrion's disease, pertussis, diphtheria, influenzal meningitis, anthrax, actinomycosis, trichomonas vaginalis vaginitis, and rat bite fever. In addition to use against these specific infections, these antibiotics have found wide use in ophthalmology and in oral surgery and dentistry.

This is indeed an imposing list. However, a second line of defense against a variety of infections is also available. Tyrothricin, bacitracin, polymyxin, neomycin, viomycin, erythromycin, carbomycin, and fumagillin all have a place in the physician's armamentarium. These often prove to be successful where the others fail. Furthermore, antibiotics just becoming available may add new ammunition in the war against infectious diseases.

I think it may be safely said that the antibiotic preparations are used as prescription drugs more frequently in treating serious and crippling diseases than any other drug or class of drugs now available. It has been conservatively estimated that in dollars spent for prescription drugs in recent years, 40 percent of all prescriptions drugs sold include one or more antibiotics.

Thus it is obvious that these drugs are of the greatest importance to the public health and that they deserve a special form of control, such as that established by the certification system. The principle on which certification of these drugs is based appears to be sound; that is, they must be certified because of (*a*) their great importance to the public health, (*b*) their use in serious and crippling diseases, (*c*) the security of a double check on their safety and efficacy given the practicing physician and his patients, and (*d*) their production by biological means, which may result in vagaries in manufacture and assay. Furthermore, the manufacturer is protected adequately from restrictive or paternalistic control by the principle that an antibiotic shall be exempt from certification when the Secretary of the Department of Health, Education, and Welfare feels that it is no longer in the interest of the public health to continue certification.

Certification of Insulin

By R. LORIMER GRANT, Ph.D.

Correct dosage is probably more critical for insulin than for any other drug. Most persons with diabetes must take insulin every day, usually injecting it themselves. A dose that is too small may lead to diabetic coma and even death; an overdose may lower the blood sugar to a level that results in an insulin shock. There are about one million known diabetics in the United States today.

These facts explain the public health importance of the Food and Drug Administration's insulin certification program, which is designed to insure, to the extent possible, that every batch of the drug will be safe and effective when used according to directions.

Insulin was the first drug to be certified by the Food and Drug Administration. Certification was not a new procedure—it had been applied to coal-tar colors for many years—but its application to drugs was new when Congress enacted the insulin amendment in December 1941. This amendment prohibits distribution of any batch of an insulin-containing drug until a certificate has been issued stating that the batch is safe and effective.

History of Insulin Control

The need for special control for insulin by the Food and Drug Administration arose from the expiration, on December 23, 1941, of one of the insulin patents. Until then, the manufacture of insulin in the United States was regulated by the Insulin Committee of the University of Toronto. Banting and Best had given the patent rights of their discovery to the university, and the university's Board of Governors had then taken out the first insulin patents and set up the Insulin Committee to administer them. The privilege of using these patents, and others subsequently administered by the Insulin Committee, was granted to several manufacturers under licensing agreements.

The purpose of the licensing agreements was to make available insulin-containing drugs of uniform and dependable potency at a minimum cost to the user. The potency of each lot of insulin was established on the basis of biological assay in two independent laboratories. The manufacturer was required to make his own assay of a lot and then to submit a sample of the lot to the insulin control laboratory in Toronto, where a second assay was made. As a further check on uniformity of product, the manufacturer was also required to send to the insulin laboratory samples from every batch of finished drug made from a lot of insulin.

The control of potency afforded by these procedures was commendable, and it was appreciated by all governmental agencies concerned with the safety of drugs. In fact, prior to 1941 the Food and Drug Administration did not have facilities for making a reliable assay of insulin potency because these drugs offered no control problems. Moreover, the Federal law was inadequate to deal with insulin drugs. The only procedure available required collection of a sample from interstate shipment, a

Dr. Grant, a pharmacologist, is chief of the Insulin Branch, Division of Pharmacology, Food and Drug Administration.

time-consuming assay for potency, and then legal action to prevent further distribution of any drug found to be unsafe. This procedure could result in grave consequences for the consumer.

As the expiration date of the patent approached, several groups, particularly the American Medical Association and the Board of Trustees of the United States Pharmacopeia, sought means to continue the special type of control for insulin that had been provided by the Insulin Committee. E. Fullerton Cook, the director of revision of the pharmacopeia, brought the problem to the attention of the Food and Drug Administration in connection with the drafting of a monograph for insulin injection which was to be admitted to the pharmacopeia after the product patent expired. The Commissioner of Food and Drugs, Walter Campbell, proposed that the pharmacopeia set up an insulin board and establish a laboratory for the testing of the drugs prior to distribution. This plan, similar to that for antianemia preparations, was rejected by the Board of Trustees of the pharmacopeia. Instead, it suggested that the monograph for insulin injection carry a requirement that no lot be released until certified by the Commissioner of Food and Drugs. This proposal was not adopted because it could not be enforced under existing law, but it served to introduce a new idea for Federal control of drugs.

To provide a legal basis for certification, new legislation was needed. Identical bills providing for the certification of drugs composed wholly or partly of insulin were introduced in the House of Representatives on December 16, 1941, and in the Senate on the following day. The bill was passed by the House on December 18 and by the Senate on December 19, and was signed by the President on December 22. This law amended the Food, Drug, and Cosmetic Act of 1938 to require that: (*a*) all insulin-containing drugs be certified before distribution, (*b*) regulations be promulgated by the Administrator of the Federal Security Agency providing for this certification on a fee basis, and (*c*) prior to actual certification of batches, those drugs tested and released by the Insulin Committee be released for distribution.

The Insulin Regulations

The procedure for certification of insulin drugs is described in regulations published in the Federal Register. The original regulations appeared February 6, 1942. These have been amended as new drugs have been added or as experience has dictated.

All the insulin regulations have been drafted in collaboration with the manufacturers of insulin and with the advice of the Insulin Committee of the University of Toronto. They provide for a continuation of the two-assay control of the potency of each lot of insulin and for the examination of samples from every finished batch by both the manufacturer and the Food and Drug Administration. The tests and methods of assay, as well as the standards to be met, are largely those suggested by the manufacturers of insulin. In other words, the industry sets its own standards, and the Food and Drug Administration enforces them.

The regulations require that the manufacturer do the following in order to have a batch of a drug certified:

1. Describe the production facilities and the controls used to maintain identity, strength, quality, and purity of each batch of drug.

2. Submit to the Food and Drug Administration for its approval a sample of the insulin to be used in the batch before he submits a batch for certification. With this sample he must submit a trial dilution of the insulin and the results of his own biological assay of the insulin. He may also send the results of a biological assay made in the laboratory of the Insulin Committee.

3. If the batch is to contain protamine or globin, obtain approval from the Food and Drug Administration of the ingredient to be used.

4. If the batch is to be protamine zinc insulin, globin zinc insulin, isophane insulin, or lente insulin, obtain approval from the Food and Drug Administration of the trial mixture which will serve as a pattern for future batches of the drug.

5. Submit samples and the results of tests of the finished drug to the Food and Drug Administration.

In administering the provisions of the regu-

lations, the Food and Drug Administration must do the following:

1. From time to time, inspect the factories making insulin-containing drugs, with special attention to the facilities, procedures, and controls applied to insulin.

2. Analyze samples submitted in connection with a request for approval, make biological assays to determine potency, review protocols of the manufacturer and of the Insulin Committee's testing laboratory, and notify the manufacturer of approval or refusal to approve the material for use in making batches of an insulin drug. If approval is refused, the Commissioner of Food and Drugs must tell the manufacturer the reasons.

3. Test samples from every finished batch of an insulin drug before issuing a certificate stating that the batch is safe and effective. These tests always include a determination of nitrogen content, which is an indirect measure of potency, and a check on sterility.

Since the manufacturer has usually completed all of his tests before submitting a sample, refusals to approve or certify are rare. Most cases of refusal to approve have involved the trial mixtures of the slow-acting insulins. The samples submitted in these cases failed to meet all the standards established to insure uniformity in the type and duration of action of the drug. An adjustment in the proportions of ingredients has usually produced a mixture that could be approved. Certification was refused for one batch of protamine zinc insulin that was found to be more alkaline than the permitted limit. This condition was evidently caused by traces of the washing solution used to clean the vials. Samples of one batch contained viable organisms, but the manufacturer found the contamination after submitting the sample and did not complete his request for certification.

As a measure of the effectiveness of control by certification, the Food and Drug Administration investigates every complaint concerning a certified drug. No complaint has been found to be due to a contaminated or faulty batch of an insulin-containing drug. All partly used samples that have been found to contain viable organisms appeared to have been contaminated by the user. No complaint of lack of potency has been substantiated. Recently, some patients ignored the label warning and used protamine zinc insulin which had become granular. Samples of the same batch kept in proper storage had a normal physical appearance. We believe that all certified insulin-containing drugs are safe and effective when they are used according to the directions on the labeling.

Organization of Control

The responsibility for certification of insulin has been delegated by the Commissioner of Food and Drugs to the Division of Pharmacology and specifically to the Insulin Branch of that division. The staff of the Insulin Branch consists of the branch chief, one chemist, two laboratory technicians, and one secretary. Laboratory facilities include one animal room, where the rabbit colony is housed and the bioassays are conducted; one chemical laboratory, where routine tests of samples are made; and the combined laboratory and office of the branch chief. These laboratories are equipped and maintained and the staff of the branch is paid from the fees collected from the manufacturers who use the certification service.

The fees for the different services vary, but the major portion of the income is from the fixed fees for certification of batches of finished products. The fee for a single batch is determined by the number of samples submitted for test. At the present time, the cost to the manufacturer is $50 for batches containing up to 50,000 vials plus $10 for each additional 10,000 vials in the batch. Any excess of income from the fixed fees over the cost of maintaining the service is refunded. Some fees depend upon the cost of the services. For services that require the use of the animal colony, most of the fee is attributable to the cost of maintaining the colony. For instance, the present cost of a biological assay for potency is approximately $1,200, more than half of which is for maintaining the animal colony.

Biological Assay Procedures

The most important test required for the certification of insulin is the biological assay for

potency. The potency may be determined by a number of methods, all of which involve a comparison of the drug being tested with a standard insulin. The methods used by the Food and Drug Administration have been the variations of the rabbit method currently official in the United States Pharmacopeia. The U.S.P. XII method required almost 1,000 determinations of blood sugar and two 5-day work weeks for completion. The test now official (U.S.P. XV) is greatly improved. It can be completed in 1 work week, and the confidence limits of the results can be calculated. It is possible, when the responses of the animals are very uniform, to make only 96 blood sugar determinations for a suitable assay, but the usual number is nearly 300.

As with all biological assays, the reliability of the assay of insulin depends on the extent of variation in response of the animals. To obtain the best results, unsuitable animals must be discarded from the colony. It is therefore essential to have an animal colony that is used exclusively for the assay of insulin and to maintain it in readiness to assay any sample submitted. A chemical method for determining potency would reduce considerably the cost and probably would increase the precision of the results, but our knowledge of the chemical structure of insulin indicates that some entirely new technique will be needed before we realize this goal.

It may appear that certification, while affording maximum protection for the user of insulin, substantially increases the cost of this essential drug and thereby adds to the burden of the consumer. However, we have calculated that the total fees collected by the Food and Drug Administration for insulin certification since the beginning of the program average less than three-tenths of a cent for each vial certified.

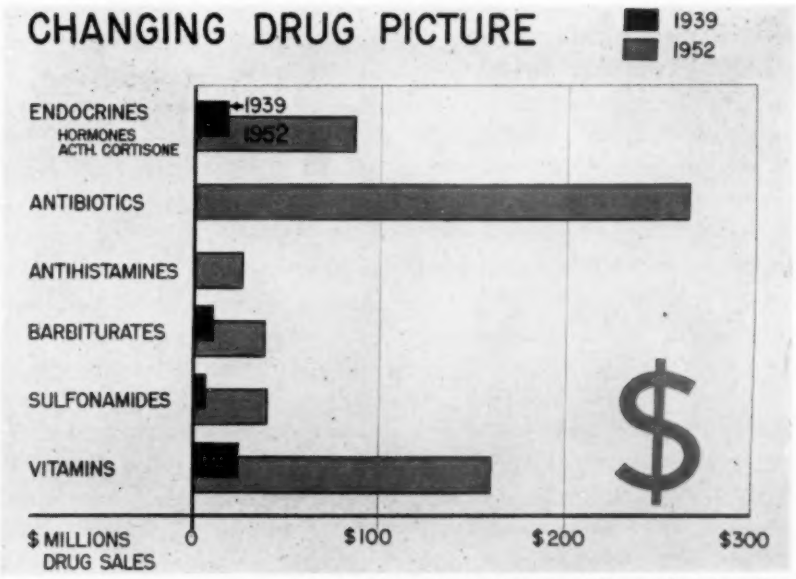


Chart from the Food and Drug Administration

Drug sales reflect advances in biochemistry. Approximately half of the total dollar value of prescriptions written today goes into antibiotics unknown in 1939. The sales of endocrines have grown from $10 million to more than $90 million. Antihistamines, unknown in 1939, have sales exceeding $25 million. Barbiturate sales have more than tripled. Sulfonamides have multiplied eightfold, and vitamin sales have increased about sixfold. Drug consumption as a whole has greatly expanded.

An assessment of the serologic response to poliomyelitis vaccine in children, following passive immunization with gamma globulin, and in tuberculous children.

Poliomyelitis Vaccine Studies

By GORDON C. BROWN, Sc.D., ALAN S. RABSON, M.D., and DONALD E. CRAIG, Ph.D.

THE RECENT demonstration of the effectiveness of the Salk poliomyelitis vaccine in actual field trials in children (*1*) has concentrated interest on active immunization in controlling poliomyelitis. Nevertheless, the use of passive immunization in the form of gamma globulin (*2, 3*) may be indicated under circumstances requiring rapid protection. Since the action of the immune blood serum is almost immediate, but of short duration, it should be possible to combine this effect with the slower but longer lasting active immunity obtained with the vaccine. Before such passive-active immunization procedures are used, however, information must be obtained that the administration of gamma globulin does not interfere with artificially acquired active immunity.

Previous reports from the virus laboratory of the University of Michigan (*4*) have shown that gamma globulin does not prevent naturally acquired subclinical infection in human beings or the subsequent development of type-specific antibodies. Mixtures of antipoliomyelitis serum and virus have previously been reported to have very little antigenic effect in animals (*5–8*), but this was probably due to the fact that the virus was actually neutralized before inoculation.

Early work with virus and immune blood serum administered separately indicated that monkeys could be immunized in this manner although the techniques utilized were hardly adequate for the quantitative measurements attempted by the authors (*9–11*). More recently, Bodian (*8*) has described experiments in monkeys receiving gamma globulin in one leg and live virus in the other leg, and concluded that there was no interference with the antigenicity of the vaccine. Howe (*12*) found that a formalin-inactivated brain tissue vaccine was antigenic in a small number of humans when gamma globulin was inoculated at another site, but none of his subjects received the vaccine without the blood derivative.

The purpose of this paper is to report the

Dr. Brown is professor of epidemiology and Dr. Craig is a research associate at the virus laboratory, department of epidemiology, University of Michigan School of Public Health. Dr. Rabson is a former epidemic intelligence officer, Communicable Disease Center, Public Health Service, Atlanta, Ga. *Their studies were aided by a grant from the National Foundation for Infantile Paralysis and by the assistance and cooperation of Dr. Edna M. Jones, associate physician, Maybury Sanatorium, and of the staff of the Wayne County Training School.*

serologic results in children given gamma globulin 3 days prior to the administration of poliomyelitis vaccine, and, in addition, to describe the results of control administrations of the same vaccine to children hospitalized with tuberculosis.

Materials and Methods

During the summer of 1954 a small quantity of poliomyelitis vaccine was made available for research purposes through the courtesy of Dr. Jonas E. Salk. This particular lot of material (lot 309) had in fact been used in some areas for the nationwide field trial in 1954, but only as a third dose in conjunction with other lots. It was also used later in the summer and fall of that year in a separate study of infants and preschool children (*13*) during which it was discovered that, after this additional time of exposure to the merthiolate preservative, an unfortunate loss of antigenicity had occurred.

For most of the children in the present studies, the poliomyelitis vaccine was administered according to the same schedule used in the 1954 field trial; namely, 3 injections of 1.0 ml. each were given intramuscularly in the left deltoid muscle. The second injection was given 1 week after the first. The third injection was given 5 weeks after the first. A small group of children, however, received only 2 inoculations. The second inoculation was given at an interval of 8 to 10 weeks after the first.

When gamma globulin was used, it was administered intramuscularly in the gluteus maximus in quantities of 0.28 ml. per pound of body weight. The globulin was from the same lot (lot 212) used in a previous study (*4*) in which maximal levels of circulating antibodies were observed in 3 days and persisted for no longer than 3 weeks following this dosage.

Passive-Active Immunization

In June 1954, 27 boys, ranging in age from 8 to 10 years, at the Wayne County Training School, Northville, Mich., volunteered for the study. First, blood specimens were taken, then the boys were weighed and inoculated with gamma globulin as described. Three days later they received the first of 3 injections of vaccine. Blood specimens were taken 2 weeks after the last inoculation, or 7 weeks after the first injection. The serums were separated and stored at 4° C. until tested. Neutralization tests were performed by mixing equal volumes of original serum dilutions of 1:4, 1:8, 1:16, 1:64, 1:256, and 1:1024 with the 3 types—type 1 (Mahoney), type 2 (MEF-1), type 3 (Saukett)—of poliomyelitis virus calibrated to yield 100 tissue culture doses per inoculum as calculated by the 50 percent endpoint method (TCD_{50}). After the virus-serum mixtures had been incubated for 1 hour at room temperature, they were placed in tubes containing cultures of HeLa cells and incubated at 37° C. Appropriate tissue, virus titration, and immune serum controls accompanied each test. Microscopic

Figure 1. Serum antibody titer changes in 27 paired serums taken from Wayne County Training School boys before and after inoculation with gamma globulin and poliomyelitis vaccine.

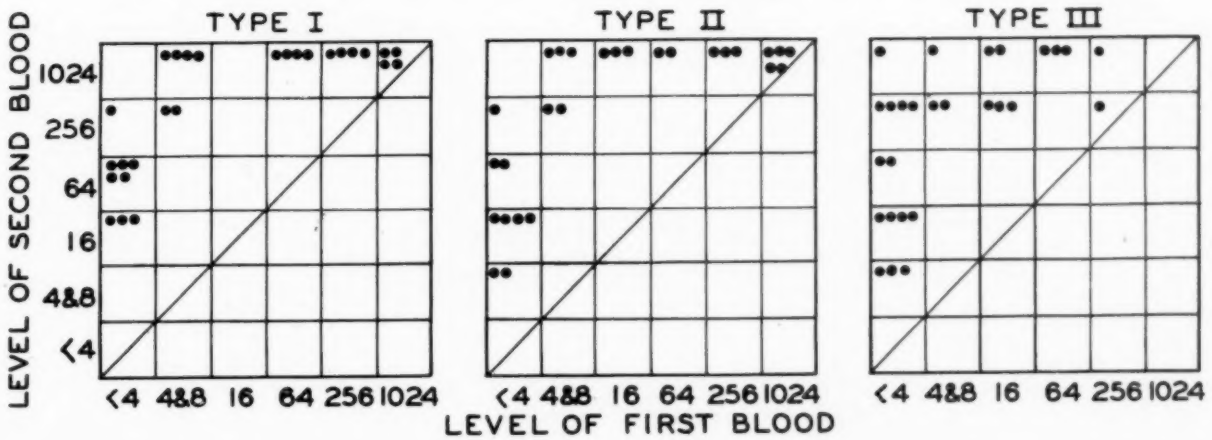
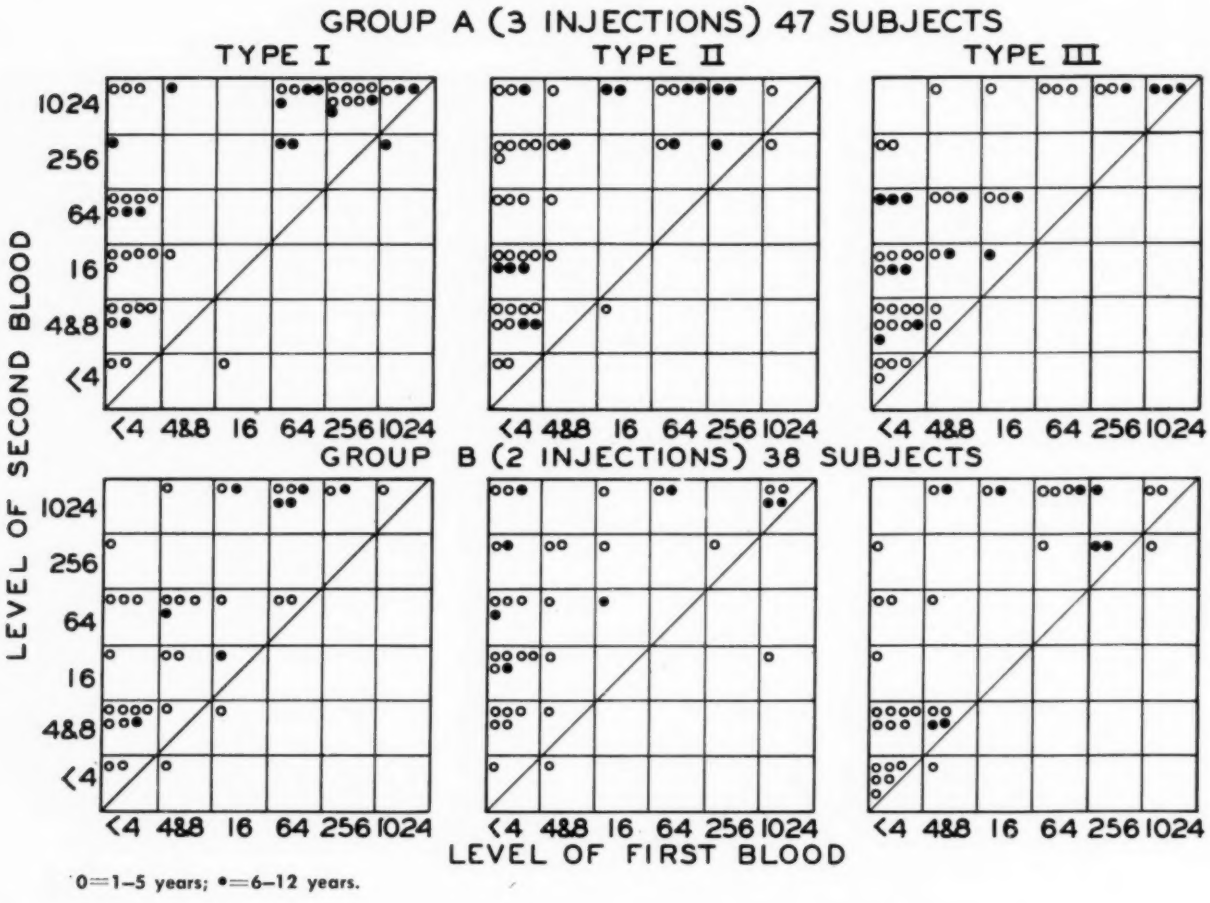


Figure 2. Serum antibody titer changes before and after poliomyelitis vaccination of 47 tuberculous children in Maybury Sanatorium.



evidence of cytopathogenicity was accepted as lack of neutralization.

The serologic response of the children who had been inoculated with gamma globulin 3 days before the administration of the first dose of poliomyelitis vaccine is shown in figure 1. In this figure the numerals at the bottom represent serum antibody levels before vaccination, and the numerals at the left indicate the titers after vaccination. Thus, any circle below the diagonal line would represent a drop in titer; any circle in the diagonal line of squares would indicate no change in titer, and any circle above the diagonal shows that the antibody titer has increased to the titer indicated on the coordinates. In spite of the small number of children studied, it is readily apparent that there was a marked increase in the serum antibody titer in most subjects as shown by the predominance of circles above the diagonal line. The median response in the children with undetectable antibodies prior to immunization was between 16-fold and 64-fold, with the more marked increase being observed against types 1 and 2 virus.

Most of the postvaccine titers of the children with demonstrable serum antibodies before vaccination reached the limit of the dilutions employed, namely 1 : 1024, and some of the titers would undoubtedly have been higher had the dilutions been extended. The controls for this experiment are represented in the results that follow.

Active Immunization

In June 1954, 85 children hospitalized for tuberculosis in the Maybury Sanatorium of the Detroit City Board of Health at Northville, Mich., were selected for study. These patients

ranged in age from 1 to 12 years with a predominance of children of 1 through 6 years. Most of the children had been nonambulatory for 6 months to a year. Blood specimens were first obtained from all; then vaccine was administered according to two schedules of inoculation.

Forty-seven children received 3 injections of 1 ml. intramuscularly at 0, 1, and 5 weeks, as given to the training school group after gamma globulin injections. Thirty-eight children, however, received only 2 inoculations at an interval of 8 to 10 weeks. Two weeks after the last injection, blood specimens were obtained from all the subjects again, and the serums were filed at 4° C. until tested.

For purposes of clarification, the children receiving 3 inoculations will be classified as belonging to group A and those with only 2 inoculations as group B. Five months after the first inoculation, blood specimens were taken from 21 group A and 25 group B subjects. Ten months after the start of the experiment, specimens were obtained again from 19 of the children (11 of group A and 8 of group B) who were still in the sanatorium, following which a booster inoculation of vaccine (lot E5721) was given, and blood specimens were taken 3 weeks later. These latter individuals, then, were children who had been studied over a period of approximately 1 year during which time 5 blood specimens had been obtained, before and after primary and secondary inoculations. All serums were tested for neutralizing antibodies, as described previously.

Figure 2 presents the serum antibody changes in the tuberculosis patients in Maybury Sanatorium after they received the primary inoculation of the vaccine. The upper part of the figure portrays the changes in the children who received 3 injections (group A), and the lower half shows the results for the group who received 2 injections. It will be seen that regardless of the serum antibody titer prior to vaccination, most of the subjects responded well. Very few persons failed to respond, and

Figure 3. Group A—Composite results of antibody response to standard virus types after 3 injections of Salk vaccine, lot 309.

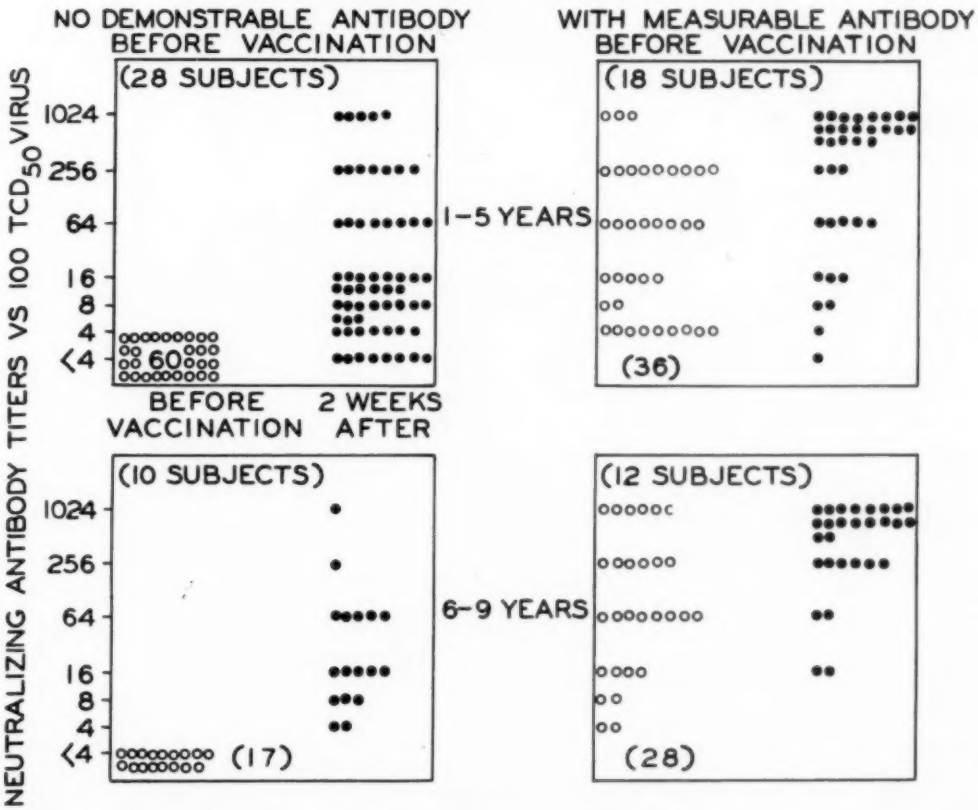
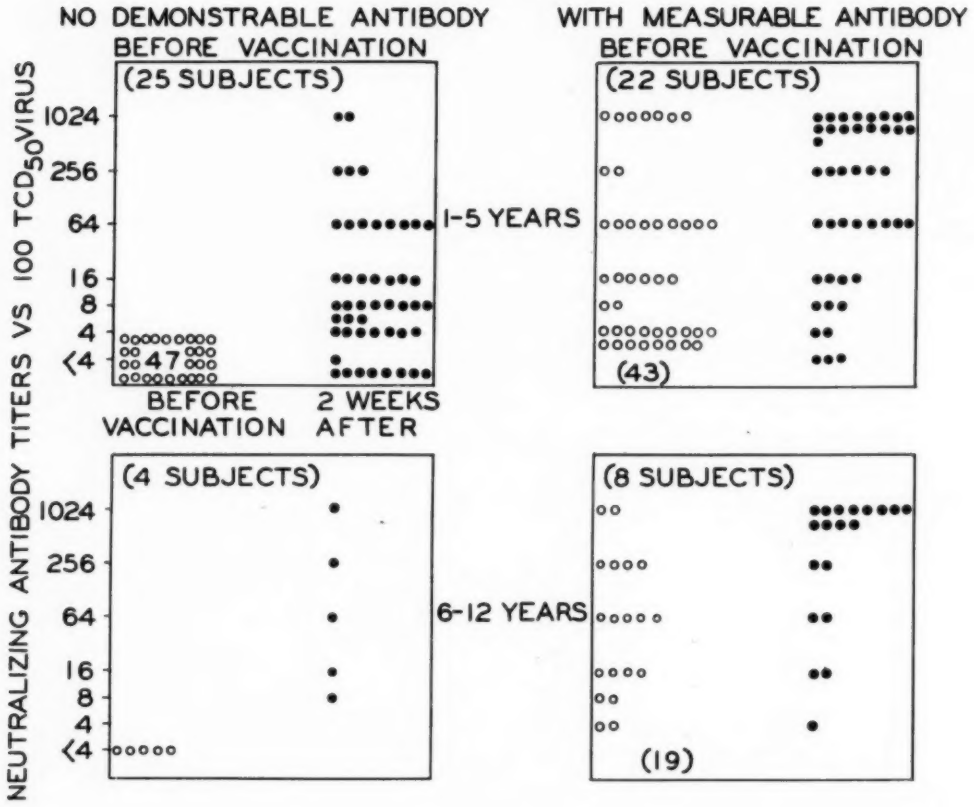


Figure 4. Group B—Composite results of antibody response to standard virus types after 2 injections of Salk vaccine, lot 309.



most of the failures are related to the type 3 component of the vaccine.

The data on the 47 children receiving 3 inoculations are reorganized as composite charts in figure 3, illustrating the development of demonstrable antibodies where none could be detected prior to vaccination and also portraying the results in the children who had antibodies before vaccination. In each of the four charts the antibody levels before vaccination are shown on the left, and the levels 2 weeks after vaccination are shown in the right-hand column. Thirty-two of the children were from 1 to 5 years of age, and, with the exception of one 12-year-old, the other 15 were from 6 to 9 years old. Thirteen children in the 1- to 5-year group had no demonstrable antibodies to any type of virus; 6 had antibodies to only 1 type; 9 had antibodies to 2 types, and only 4 had antibodies to all 3 types. Twenty-eight subjects were lacking in demonstrable antibodies to either one, two, or to all three types of virus, and the 60 such instances with the titers obtained after vaccination are shown in the upper left portion of the composite chart (fig. 3). A median antibody titer of 16 was observed. This duplicates exactly the median antibody response to vaccine in the 10 subjects of the 6- to 9-year age groups having 17 instances of no antibodies before vaccination although the younger age group appeared to have fewer antibodies initially. In those individuals with measurable antibodies to a given type of virus, the increase in the 1- to 5-year age group from a median of 64 before vaccination to a median of 1,024 after vaccination is again duplicated exactly in the older group.

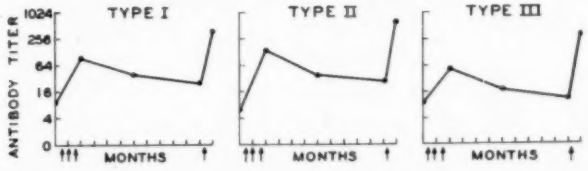
Figure 4 represents the composite results of antibody changes in children receiving only 2 injections of vaccine. Thirty of the subjects were from 1 to 5 years of age, and only 8 were from 6 to 12 years old. Eight children in the 1- to 5- year group had no demonstrable antibodies to any type of virus, 6 had antibodies to only

1 type, 11 had antibodies to 2 types, and only 5 to all 3 types. The composite chart shows that, when antibodies were not present before vaccination, the median rise in homologous titers was eightfold. In the 22 children 1 to 5 years old with 43 instances of demonstrable antibodies to virus (upper right of the chart), the median homologous titers changed from 16 before vaccination to 256 after vaccination, a 16-fold increase. The number of children in the 6- to 12-year age group was too small for accurate analysis, but the antibody increases in these few are obvious and of the same order.

As mentioned previously, blood specimens were obtained from 46 subjects in the study 5 months after the first inoculation of vaccine. Neutralization tests with these serums showed a median fall in antibody titer against all 3 types of virus regardless of whether the children had received two or three inoculations. The decrease was most marked in the type 1 antibodies and least in the type 3. The primary response to the latter had been less, however. This progressive decrease in measurable antibody is further emphasized in figure 5, which shows the geometric mean of the antibody levels in a series of 5 serums taken over a period of almost a year in those subjects who received 3 inoculations of vaccine at the times indicated by the first 3 arrows and a subsequent inoculation 10 months after the start of primary immunization, as indicated by the single arrow.

The tests revealed a good primary response to vaccination, followed by the gradual decline over the intervening 10 months to a point only slightly greater than that seen before vaccination. The effect of the secondary inoculation in these children, however, was quite pronounced and might have been numerically greater had the test dilutions been extended since many serums neutralized 100 TCD_{50} of virus at the highest dilution employed (1:1024). The titers following the secondary vaccination in all children against all 3 types of virus were much higher than before vaccination, and in many persons the increase ranged from less than 1:4 to greater than 1:1024.

Figure 5. Geometric mean of antibody level in 19 tuberculous children (groups A and B, Maybury Sanatorium) bled 5 times during interval from before vaccination to after receiving poliomyelitis booster injection.



Discussion

The extent of the serologic response in children inoculated with gamma globulin 3 days prior to the first injection of poliomyelitis vaccine proves definitely that this dosage, which is twice that usually administered to humans, does not interfere with the development of active, artificially stimulated antibodies. The titers induced in this study were judged to be more than adequate when compared with the titers obtained following vaccination in the field trial of 1954 and when compared more specifically with titers in tuberculosis patients receiving injections from the identical lot of vaccine, on the same schedule and at the same time. These antibody titers reflect the response to the vaccine itself and not the residual passively acquired antibodies of the gamma globulin since previous studies with identical quantities of the same lot of gamma globulin injected in persons without previous antibody showed that only very low titers of antibody not exceeding 1:4 could be detected and then for a period not more than 3 weeks after injection. Thus, the conclusion is inescapable that poliomyelitis vaccine is capable of inducing the formation of antibodies quite uninfluenced by the presence of circulating artificially acquired antibodies. This observation has importance in view of the possible epidemiological circumstances which might indicate the advisability of a course of passive-active immunization in human beings.

The results of vaccinating patients hospitalized for tuberculosis not only serve to control the above results inasmuch as the lot of vaccine and the schedule of inoculation were the same but also illustrate the immunological response to a virus vaccine in nonambulatory persons infected with a debilitating bacterial disease. The 16-fold response to primary vaccination regardless of the existence of demonstrable an-

tibodies before inoculation shows that children hospitalized for tuberculosis are equally as good subjects for immunization as are normal children. In fact, the importance of immunizing institutionalized persons is emphasized by the frequency with which epidemics have occurred under such conditions. In this very hospital, 12 cases of poliomyelitis occurred among 80 children in 1952, 2 years prior to this study.

As expected, there appeared to be no correlation whatsoever between the individual antibody responses and the character or extent of the tuberculosis. Furthermore, the response of the young children between 1 and 5 years of age was judged as good as that of the older children regardless of whether they received 2 or 3 inoculations of vaccine. This important observation of the efficacy of vaccine in the younger age group is a forerunner of more extensive data representing studies in infants and preschool children (*13*) to be published soon from this laboratory.

The gradual decrease in antibody titer during the period following primary vaccination has been described elsewhere (*14–16*), but the sharp booster effect of subsequent inoculations in the individuals in this study not only demonstrates the beneficial effect of the booster but suggests strongly that, regardless of the level of demonstrable antibodies at that time, significant immunization did persist after the primary stimulation.

Summary

The serologic response of children inoculated with gamma globulin 3 days prior to active immunization with poliomyelitis vaccine was measured by the virus laboratory, University of Michigan School of Public Health. The consistent rise in antibody titer in the children in the study demonstrates that passive immunization of this extent has no suppressive effect on the individual's response to the vaccine.

The vaccination of children hospitalized for tuberculosis resulted in antibody levels consistent with the response of normal children and indicated that immunization of tuberculous individuals should be practiced. The effect of 2 inoculations was equally as good as that of 3 injections, and no significant difference was observed in the response of 1- to 5-year-old children as compared with that of older children, 6 to 12 years of age.

The booster effect of secondary vaccination almost 1 year later is demonstrated and discussed.

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Increase in Nuclear Reactors

The number and heat capacity of nuclear reactors in the United States, used to generate electric power, will increase predictably, according to the Division of Sanitary Engineering Services, Public Health Service. There will be a parallel increase in the quantity of radioactive byproducts, it is said, with a corresponding need for protective practices.

The first reactor began operation in 1942. By the end of 1955, there were 22 reactors in operation, with a heat capacity of 100 megawatts. As of February 1956, approximately 40 nuclear reactors, about one-half of which are for the production of nuclear power, were in some stage of design or construction. Seven new reactors, with a heat capacity of 90 megawatts, are expected to begin operation during 1956.

Radioactive wastes from reactors must be segregated or diluted to tolerable concentrations. At present, underground storage and ocean burial are among the methods used or proposed for segregation. Both the economy and the adequacy of these methods are under continuing investigation in anticipation of the probable increase in volume of radioactive wastes.

It is estimated that nuclear power plants completed during 1964 alone will have a power level exceeding 2.25×10^6 kilowatts, producing wastes each year of 3.3×10^{10} gallons containing 10 millicuries per gallon. An indication of the magnitude of this activity is that the entire flow of the Mississippi River would not be sufficient to dilute to permissible concentrations the fission products from these plants. Such a method of dilution, of course, is obviously least likely to be used.

Hospital Problems of Mass Evacuation

By HAROLD M. ERICKSON, M.D.

HOSPITALS, particularly those in target areas to be evacuated, have one of the most important and yet most complex roles of any group in civil defense. Removal of persons who are ill or who are recovering from injury is obviously a much more difficult job than moving able-bodied persons. This, however, is not the only problem of the hospital. Arrangements must be made for continued care of hospital patients either in expanded hospitals at a relatively safe distance from the civil defense impact area or in an emergency hospital. Either or both must be established by the hospital staff with the aid of whatever mobile hospital teams might be available.

Natural disasters as well as manmade disasters may require mass evacuation. Fire, flood, earthquakes, tornadoes, and hurricanes are always with us. One can scarcely pick up a newspaper or turn on a news broadcast without hearing of a disaster some place in the world.

No hospital is free from the possibility of having to evacuate, and, certainly, every hospital may be involved with the care of patients who have been evacuated or with those who become ill or are injured during an evacuation.

During "operation greenlight," a practice evacuation in Portland, Oreg., in 1955, 100,000 persons were evacuated from the downtown area in 34 minutes. This shows what can be accomplished through careful, advance planning. But it was not a test for Portland hospitals since none of them were evacuated.

Dr. Erickson, Oregon State health officer, delivered this paper at a meeting of the Oregon Association of Hospitals in October 1955 at Gearhart, Oreg.

Imagine a real alert at 3:00 o'clock in the morning instead of 3:00 in the afternoon, with a howling wind and heavy rain falling and darkness blanketing the area. What would happen at the hospital? Most of the Portland hospital administrators would probably be at their homes fast asleep. On awakening, what would be the administrator's first thought? Could he reach the hospital? If not, who would be in charge? Is there a plan for evacuation that is well known to all of the staff, or would chaos develop and removal of patients be impossible because there had been no advance planning?

An evacuation experienced in Oregon during the Vanport flood in 1948 will illustrate what can happen in a disaster. Fortunately, the Vanport Hospital had been evacuated in advance, but some 15,000 to 20,000 people were still housed in Vanport on that Memorial Day afternoon. In Portland, adjacent to Vanport, several of the Red Cross staff members and I were in the offices of the Multnomah County Chapter of the American Red Cross planning the evacuation of Vanport. The weather was ideal. At 4:00 p. m. our planning was interrupted by word that a railroad fill, holding off the flood waters of the Columbia River, had given way, and the city of Vanport, built to house 40,000 to 50,000 people, was being engulfed by a flood of water.

Pandemonium soon broke loose in the chapter offices. Telephone lines were completely blocked by incoming calls. Volunteers jammed the offices. The first thought of the chapter's medical department was of infants and small children. Milk and baby food were ordered through the chapter, but we were helpless to do much more without communications.

The director of the medical department and

I walked to the offices of the Oregon State Board of Health a few blocks away. In a short time we had a large number of the health department staff on duty. A switchboard operator and eight trunk telephone lines were available to us, but we could not make efficient use of them because we had no communication with the Multnomah County Chapter, and we finally went back to that office. There we learned that a request had come through for 20 physicians to report in the neighborhood of Vanport. We did get calls through to a number of doctors, but to this day I do not know whether they were able to reach the area since the streets and highways in the vicinity, we learned later, were completely blocked both by cars that were fortunate enough to get out of Vanport and by sightseers and others trying to reach the scene. In the excitement, it took only one or two stalled cars to block the limited number of roads out of Vanport. Hundreds of cars were completely flooded over; two-story houses were washed hundreds of feet off their foundations—many of them collapsed. But fortunately, only 19 persons lost their lives. There were very few, if any, injured.

At 10:30 that evening the milk and baby food we had ordered were available for delivery to the shelters. Two nurses and I were designated to make the rounds of the some 20 shelters within Portland. That was an enlightening experience. As we reached the various shelters, we found in most instances that babies as well as other evacuees had been fed. People were lined up for blocks near the shelters—not to receive aid but to offer blankets, clothing, food, and their own homes for housing the evacuees. During the first 2 or 3 days, irrespective of race, the majority of the evacuees were housed in private homes. One school was designated for the care of infants and children who needed special medical and nursing supervision. A number of children had measles and there were other illnesses. One outbreak of food poisoning resulted from hasty preparation of sandwiches and lack of refrigeration facilities in one of the shelters.

In brief, during the first few hours communications and transportation broke down, and the residents of the area were entirely dependent on their own resources. From this experience, I believe we can rely to a great extent on the ingenuity of people and on volunteers if a disaster is not too great. In this instance, a population of less than 20,000 had all the resources of Portland, a large city of more than 350,000, to give aid. After 48 hours, the American Red Cross, Portland Housing Authority, and many governmental and volunteer agencies together did an outstanding job of rehabilitation.

In New Jersey, the experience of the Perth Amboy General Hospital in two disasters is worth review (*1–3*). Hospital officials met the first, a munitions explosion on four lighters at the South Amboy docks in 1950, with a plan for emergency accident patients, drawn up the month before. The plan worked moderately well, and, with its flaws remedied, the hospital was really prepared for the second disaster, a railroad wreck in 1951.

Certainly we can profit from experiences in disaster, particularly from the experiences of hospital administrators (*1–8*). In the hospital reports, one statement appears time and again: "Advance planning for disaster is essential if unnecessary loss of life is to be prevented and the needs of patients are to be taken care of in an emergency; there is no substitute for advance planning.

In an evacuation of the Portland metropolitan area, as in any other city the same size, 500,000 persons would have to be moved out. Portland hospitals would have to transport some 3,000 patients; 1,300 of these would be surgical cases and 300 serious medical cases. There would be approximately 100 obstetrical cases, 150 newborn infants, and perhaps 10 or more premature babies that would require special care. In addition to these, a portion of the 2,500 persons who become ill each day would require hospitalization and would have to be cared for. It is estimated that at least 5,000 persons would require first aid or even hospital care as a result of injuries incurred during the evacuation. An additional 3,000 to 4,000 beds would be needed. All of the supplies and equipment would have to be provided locally, at least during the first 24 hours or so until the hospital supplies stockpiled by the Federal Civil Defense Administration could be made available.

The Questions

What then are some of the specific problems faced by the hospital administrator? Getting back to the warning at 3:00 a. m. on a stormy night, with 4 to 6 hours expected before an attack, problems would be:

1. How will staff members be notified? Which ones should be called and who should notify them?
2. Which patients are to be evacuated and which must be left because they are in too critical a condition to be moved?
3. Where will the critical patients be moved to in the hospital?
4. Who will be left in attendance?
5. Where will the patients that are being evacuated be transported to?
6. Which patients will walk out of the hospitals and by what route? Where do they report? Who directs their leaving?
7. Will helpless patients be moved by stretcher, litters, or wheelchairs, or will beds be moved?
8. Who accompanies the patient?
9. If power fails, is there provision for emergency lighting? What substitutes are there for power?
10. How do we avert panic?
11. Who sets up the temporary hospital, if that is necessary?
12. Where will supplies and equipment be obtained? Where will staff be obtained?
13. How will the staff and patients be fed?
14. What sanitation facilities will be used?
15. What records are essential?
16. How will relatives and other interested persons be notified?
17. Will mortuary services be available? How will the dead be cared for?
18. Who will assume responsibility for various activities if key persons are not available?
19. Can volunteers be used?

These are some of the questions the administrator of the hospital in the evacuation area would face. The hospital outside of the impact area would have additional problems.

Administrators of the receiving hospitals may be warned that patients are being brought to their hospitals. Without prior planning, however, their first knowledge of evacuation might be on the arrival of patients. These hospital administrators would face additional problems:

1. How will traffic be controlled outside the hospital and inside the hospital?
2. Where are the keys to the various services?
3. What areas of the nonevacuated hospital are to be used for the screening of patients, first aid, additional surgeries, wards, and other necessary emergency services?
4. Are additional hospital supplies and equipment available? If so, where? How will they be obtained? How transported?
5. Where can additional blood and blood plasma be obtained in an emergency?
6. What will be done about supplies and equipment that are offered to the hospital?
7. How will relatives, visitors, and the press be handled?
8. How will admissions and discharges of patients be handled and recorded?
9. Will orderlies and housekeeping personnel as well as other key personnel have transportation to the hospital?
10. Will staff members and pretrained volunteers have personal identification to allow passage through road blocks and guarded centers?

I'm sure that hospital administrators will think of many more questions that need answers. We all realize that order or chaos in an emergency will depend on whether or not these questions have been considered and plans made in advance. Again, and we cannot emphasize it too often, advance planning is a must.

Planning Principles

What are some of the principles of planning? Briefly outlined, they are:

1. Anticipate the worst possible disaster that might strike the hospital without completely destroying it and plan for this. The resulting plan will enable the staff to handle lesser disasters more effectively.

2. Cooperative planning is best. Bring as many hospital staff members as possible, including the medical staff, into the planning. Forming the nucleus of the planning group may be the hospital administrator, the medical chief of staff, and the director of nurses. A trained public health worker might be invited to join

this group. Other staff members can be called upon when planning in specific services is required.

3. Develop a simple and flexible plan. You cannot plan for every disaster, but a simple, flexible plan can be easily modified as the exigency demands.

4. Correlate the hospital plan with that of the local civil defense agency, fire department, police department, health department, and other agencies that might be concerned.

5. Plan for communications. Arrange for messenger service and two-way radio as substitutes for the telephone, if it should be out, and have a battery-operated radio set available. In planning notification of staff members, remember that the switchboard operator can call only a limited number of persons. Chain-type calling has proved of value.

6. Provide for emergency lighting, water supply, and sanitation facilities.

7. Consider making available a helicopter landing strip at the hospital or nearby.

8. In stocking supplies, some hospitals that have experienced disasters planned initially on having at least 1 month of supplies on hand. Now, the same hospitals are planning on 2 to 3 months of supplies, which they believe will take care of the average disaster. The issuance of moderate amounts of supplies during the emergency and moving them in boxes has been of value in conservation. Get information on reserve medical supplies and equipment available from other hospitals or medical facilities in a nearby area.

9. Keys labeled for all essential parts of the hospital and placed together in a locked box that is to be opened only in an emergency has been a demonstrated aid.

10. Decide on essential records, their preparation, and routing. Designate a responsible staff member and alternates to list daily evacuable and nonevacuable patients.

11. Arrange for emergency mortuary services.

12. A list of volunteers should be considered. It has been pointed out, however, that unless the volunteers are recruited in advance and trained and oriented as to their function in a disaster, they may be of little use. They may, in fact, be a handicap.

13. Plan emergency housing and feeding for the staff, including volunteers. Determine source of food supplies.

14. Assign in writing responsibilities, duties, and priorities of functions to each staff member and pretrained volunteer, designating as many as five alternates for each key position.

15. Avert panic. Psychiatrists tell us that the best way to prevent panic is to give everyone concerned a job to do, familiarize him with the job, and let him do it in the disaster. Combating rumors and giving people an opportunity to discuss their fears and problems is the best approach to psychiatric first aid.

16. Have a check list. Be sure that all details have been considered.

17. Familiarize the entire hospital staff with the plan.

18. Conduct realistic exercises that are as complete as possible.

19. Review the disaster plan and amend it as needed.

These are some of the general principles—a skeleton outline to be enlarged upon and filled in with many administrative details.

To quote from a conclusion reached at a recent meeting in Chicago called to plan for disaster in schools: "Manmade disaster may come and go, but natural disaster is always with us; let's be prepared."

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The Biology of Northern Mosquitoes

By W. C. FROHNE, Ph.D.

IN the last 10 years, northern Canada and Alaska, the continent's northwestern defense front, have witnessed a construction boom. In this mosquito-infested arctic wilderness, military bastions, power dams, and metallurgical plants are being erected, and oil fields and mines are being developed. A major handicap to this growth has been the seasonal swarming of mosquitoes.

Both the Canadian and United States Governments have directed scientific studies of these insects to establish their importance to public health and to improve the contributions of entomology to polar medicine.

Canadian entomologists and personnel of the Arctic Health Research Center have pushed back the frontiers of Alaskan insect lore and have provided basic biological contributions to knowledge of mosquitoes. A few years ago they discovered a hitherto unrecognized type of life cycle characteristic of many arctic mosquitoes. This discovery will serve, in conjunction with another well-known cycle, as a framework for this discussion.

The role of the northern biting Diptera, including mosquitoes, as disease vectors is largely unexplored. No one has undertaken even a pioneering general survey of pathogens associated with northern mosquitoes. Polar medical entomology today is reminiscent of the status of tropical medical entomology 60 years ago. However, studies of mosquito-borne encephalitis are progressing in Saskatchewan. In Sweden, *Aedes cinereus*, a mosquito abundant in Alaska as well, was recently shown to spread tularemia. Also, in subarctic Siberia, Russians have demonstrated that mosquitoes transmit malaria and Japanese B encephalitis.

Research on disease agents associated with man and mosquitoes in the far north might reveal important pathogenic counterparts to those in temperate and tropical zones, including many only recently detected. However, at present, northern Diptera are regarded primarily as biting, bloodsucking pests.

Dr. Frohne is chief, Entomology Activities, Arctic Health Research Center, Public Health Service, Anchorage, Alaska.

Northern Biting Insects

In Alaska and other northern countries, the Diptera include the most offensive insect species. Of all bloodsuckers, the more than two dozen mosquito species are the worst.

We omit lesser offenders, of which the major groups are: (*a*) Heleidae, punkies or no-see-ums, about 12 species, half of them undescribed, of the genus *Culicoides*; (*b*) Simuliidae, or blackflies, of 36 described species; (*c*) Leptidae, or snipeflies, 2 redoubtable, little-known species of *Symphoromyia* resembling horseflies; (*d*) Tabanidae, horseflies and deerflies, an uncertain number of forms, perhaps 20. Like the better known mosquitoes, the punkies and flies are important because the females bite man.

Need for Mosquito Control

Following the lead of military medicine, and especially the counsel of the late Dr. Joseph Mountin of the Public Health Service, health workers accept mosquito abatement as adjuvant public health. Culicidology is one of the acknowledged health sciences.

During Alaska's summer, hordes of mosqui-

This welcome article brings together diverse information, some of it quite new, about the insect fauna of the far north, more information than has been assembled in one place before. It also highlights the paucity of our knowledge about these species, which are such powerful deterrents to the development of Alaska and which must be subdued if the natural resources of that vast land are to be exploited.

Virtually nothing is known about the disease-vectoring potentialities of arctic biting insects. Indeed, little has been learned about their feeding habits. It seems unlikely that the insects could transmit disease unless they engorged with blood at least twice, with the last feeding upon man. Single broodedness seems to be the rule among the northern mosquitoes. This suggests the probability of single feedings. Yet some of the mosquitoes live more than a year, and it would seem necessary for them to have more than one blood meal to sustain normal metabolic activities even though much of the time is spent in hibernation. Probably many, if not all, hematophagous species do feed more than once.

But whether these creatures spread disease from lower animals to man, or from man to man, or whether they have nothing whatever to do with spreading disease, their overpowering numbers and vicious biting habits make insect control an almost necessary prelude to land development. To imply that they are unimportant from a health standpoint simply because they are not known to transmit infectious organisms is to discredit the basic tenet of the World Health Organization Charter. Thus, insect control becomes an essential function of health organizations in bringing about relief from severe insect pestiferousness.

—By JUSTIN M. ANDREWS, Sc.D., *associate chief for program, Bureau of State Services, Public Health Service.*

toes attack every exposed warm-blooded animal. Certain mammals, for example the caribou, make long annual migrations to escape them. As for man, it may well be that mosquitoes more than maladies have impeded settlement of the vast and beautiful Alaskan central valleys blessed with fish, timber, and cultivable soil.

In accordance with an ecologic principle that toward the poles species increase quantitatively but decrease qualitatively, myriads of mosquitoes of a few arctic kinds attain densities rarely approached in warmer parts of the world. Man survives the polar winter by protecting himself from frost, the summer, only by antimosquito measures. Evidently, scientific control of arctic mosquito pests is needed to facilitate orderly development of Alaskan resources.

Life Cycle Types

To compare arctic mosquitoes with those in warmer latitudes, it is unnecessary to present the customary annotated list introducing the 20-odd *Aedes*, 5 or 6 *Culiseta*, 1 *Anopheles*, and 1 *Culex* which comprise the Alaskan mosquito fauna. Someone might be misled by apparent similarities of the Alaskan assemblage of species to stateside lists. The Alaskan list is a selected biota of peculiarly cold-tolerant forms. All belong to one or the other of two dissimilar types of northern life cycles.

Alaskan mosquitoes are invariably single brooded; there is but one generation per year. The three many-brooded life cycles characteristic of almost all mosquitoes of the United States do not occur at all, so far as is known, in the Territory.

The members of a life cycle type resemble each other in essential habits, but the species do not necessarily belong to the same genus. However, one of the northern life cycles does comprise all the species of *Aedes*. The other includes a taxonomic miscellany of the three other genera. It is sound ecology and helpful toward understanding their biologies to classify the mosquitoes by life cycle type rather than to view them as a list of scientific names.

The *Culiseta impatiens* type of life cycle was recognized as new, by the Arctic Health Research Center laboratory, from the peculiar habits of the long-lived females of a captive colony, the first such colony of northern mos-

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quitoes to be established (*1*). It was designated the *C. impatiens* type when single broodedness and obligatory hibernation of the female, a new combination, were proved. No temperate or tropical mosquito biologies like this have been described.

Some authors have observed the nonbiting habit of first-season females, others the viciousness of second-season hibernators of this species, and as a result the literature is cluttered with contradictory appraisals of *C. impatiens* as a pest.

It was soon obvious, from otherwise puzzling field data, that *Culiseta alaskaensis*, as well as the local *Anopheles* and *Culex*, shares the new type of life cycle (*2*). In this cycle the habits of females are sharply divided between the two summers they live. Courtship and mating take place the first summer, engorgement and oviposition the second. An adult *C. impatiens* female survives 10 or 12 months. After mating, the females find shelter for diapause. This rest period of estivation and hibernation lasts as long as 10 months in nature; it is as brief as 3½ or 4 months in the laboratory colony where it ends abruptly with many females spontaneously rousing to seek blood.

Normally, the blood lust appears concomitantly with increasing light in early spring, and the hibernators will bite at near freezing temperatures in order to develop and lay the egg rafts about 2 weeks later. The comparable preoviposition period of *C. alaskaensis*, however, averages much longer, 32.1 days. In both instances the preoviposition periods are unprecedentedly extended as contrasted with those of temperate zone mosquitoes. *Culiseta inornata* of the northern United States requires only 5.3 days (*3*). Many tropical *Anopheles* actually engorge, develop, and lay eggs all within a 24-hour period.

The preoviposition periods of *C. impatiens* and *C. alaskaensis* were not curtailed under experimental conditions at temperatures above 20° C. Such abnormal warmth merely caused excessive mortality. Eggs, larvae, and pupae of forms subject to the *C. impatiens* cycle develop without diapause in relatively warm permanent or semipermanent waters.

Another cycle characteristic of all Alaskan northern *Aedes* was made known by Wesenberg-Lund of Denmark 35 years ago (*4*). He designated it the *A. cinereus* cycle. Hibernation takes place in the egg, and all the forms are obligatorily single brooded. Larvae, and sometimes the pupae, tolerate cold well. *Aedes communis*, for instance, can develop normally in water as cold as 2°–3° C. Females of this type mate, engorge, and oviposit within a few weeks after emergence in May or June. Eggs are laid in drying basins of vernal pools or along the dried margins of less transient standing waters.

Cold Resistance

Pronounced cold resistance characterizes winter and spring stages of northern mosquitoes, namely, the eggs of *Aedes* and the adult females of other genera. At these stages the pests withstand months of heavy frost and the fluctuating temperatures of spring breakup. Activities of the adult hibernators are also surprisingly independent of moderate cold above freezing. *C. impatiens* females have been observed in January and February frisking on the wing and resting on the snow.

However, specific differences of degree of cold tolerance significantly distinguish the less adapted stages in both cycles. The score or so of *Aedes* can be arranged naturally in serial order based on water temperatures typical for a critical advance in stage: (*a*) temperatures at which the eggs hatch; (*b*) temperatures characteristic of mass pupation; (*c*) the seasonal order of appearance of the species on the wing. Whether the criteria used be (*a*), (*b*), or (*c*), the resulting arrangement is practically the same. Larvae of the earliest species may precede the latest in subarctic Alaska by 2 months (*5*). Thus the observer dips the former from bleak snow-melt pools after cracking the ice cover of the preceding night, whereas he encounters the latter during the bright, warm days of lush new foliage in early summer.

However, surveys which classify mosquito species according to breeding area, region, and elevation rather than by collection data are particularly instructive. Lumped records for a given species from different habitats may be deceptive where there is thermal individuality dependent on size, exposure, source, and depth of breeding waters as well as their altitude and

latitude. Unexpected contrasts in optimal temperature ranges sometimes isolate the most closely related species. For example, *A. communis*, one of the earliest larvae thriving in the lowest temperature range is nevertheless close taxonomically to *Aedes pionips*, a late warm-water larva. Larvae of all forms manifesting the *C. impatiens* cycle presumably never tolerate cold as well as any of the *Aedes*, and larval cold tolerance is thus closely bound up with life cycle type. Cold tolerance and cycle type are not only implicated in larval habitat preference, but also in geographic distribution (*6*).

Distribution

Geographers define arctic, subarctic, and temperate regions by physical criteria stressing winter cold and latitude, such as January isotherms and distribution of permafrost. To explain insect distribution in Alaska, zoogeographers must emphasize vegetation types and warmth during the all-important summer. Otherwise the terms arctic, subarctic, and temperate have practically no meaning.

The Territory is mountainous, and alpine arctic islands above the low timberline at 1,500–2,000 feet are strewn helter-skelter over temperate and subarctic regions. Moreover, without regard to elevation, there are vast remnant glaciers of the Pleistocene ice sheets which chill "temperate" southeastern Alaska. (These ice sheets never covered the arctic and melted in most of the subarctic at the time they receded from the northern United States about 5,000 years ago.)

For example, although southeastern Alaska is designated "temperate" because of the mild winter climate, its cool summers limit the fauna to hardy forms. In the warmer subarctic, where maximum summer temperatures are 90°–100° F., southerly species, such as sun-loving *Anopheles* occur. Finally, "arctic" treeless tundra extends far into the subarctic in western Alaska and merges with the Aleutian grasslands at the latitude of temperate southeastern Alaska.

In the arctic there are wooded valleys of spruce, willow, and birch representing to the biologist simply subarctic inclusions comparable to the arctic alpine inclusions. In fact, the "hemiarctic" zone proposed by Rousseau, which means demarcation between arctic and subarctic, may constitute a broad band of transitional parkland (*7*).

Trees are an important part of the environment to mosquitoes. Culicidologists conveniently designate forest forms "woods" mosquitoes. Species of open country are "tundra" or "prairie" mosquitoes. There is a sound ecologic basis for the practice. As more is learned about the distribution of northern mosquitoes in forest or treeless areas, apparent contradictions are resolved. It is essential to stress local habitats and to soft-pedal climatic regions for progress in understanding distribution. Nevertheless, interesting contrasts of arctic, subarctic, and temperate lists of mosquitoes may be made with reference to their qualitative and quantitative compositions, biologies, seasonal histories, and the practical importance of some species as pests.

Arctic Fauna

Several excessively abundant so-called dark-legged species of *Aedes*, especially *communis* and tundra forms of the *punctor* complex, are the most important arctic mosquitoes (*8*, *9*). When *Culiseta* occur at all there they are scarce and restricted to wooded valleys. *Culex* and *Anopheles* are absent, and any importance of the *C. impatiens* type of life cycle is academic in the arctic. For this reason, too, the mosquito-biting season lasts less than a month, even though at peak it is probably the most intense in the world.

Subarctic Fauna

The rich and varied subarctic mosquito fauna contains about 2 dozen species belonging to both of the northern types of single-brooded life cycles. The very large *Culiseta* pests of early spring are joined during May and June by 8 or 9 small dark-legged *Aedes* and later further reinforced and replaced by about as many, typically larger, banded-legged kinds. Two retiring and local *Anopheles* and *Culex* species at their northern limits emerge in midsummer. Over vast areas the mosquito-biting season extends from late April to early August, or nearly 4 months. Mosquito densities are high in the interior valleys and locally along the coast at

mouths of streams, causing severe pest problems in the flat areas most desirable for human habitation.

Temperate Fauna

The so-called temperate southeastern Alaskan mosquito fauna is rather similar to the subarctic list shortened to a dozen species (*10*). *C. impatiens* appears early (March) in hordes. *C. alaskaensis* occurs only as far south as Haines, the northern gateway to southeastern Alaska and the sole locality in the region for *Culex*. *Anopheles* is absent, too, so far as known. In compensation, two Californian species of *Culiseta*, *incidens* and *maccrackenae*, have entered from the south. Either species may pursue a temperate zone life cycle; be multibrooded or have larval hibernation. Unfortunately, both species are rare and their biologies uncertain in Alaska.

The mosquito-biting season in southeastern Alaska is approximately 5 months, but pest problems are markedly local and are almost always due to forms of the *A. punctor* complex, for example, *Aedes punctodes*, a salt marsh breeder. The dark-legged species with, of course, the *A. cinereus* cycle, thus so predominate that southeastern Alaskan mosquitoes, both taxonomically and biologically, resemble the arctic and subarctic faunas rather than typical temperate zone mosquito faunas.

Mosquitoes of all three life zones in Alaska are different from most stateside mosquitoes, but as they have a great deal in common, it seems logical that they be studied and controlled from a central headquarters in subarctic Alaska.

Larval Habitats

Definition of the typical larval habitats of insects harmful in adult stages facilitates further biological study and makes species sanitation feasible. As an extreme example, for many years Alaskan entomologists have been stymied in studies of the common snipefly pest, *Symphoromyia atripes*. They could not find its breeding places, immature stages, or the males. In 1955, however, the first newly hatched Alaskan *Symphoromyia* appeared in emergence traps put out in mountain meadows for sampling alpine insects. It is at long last reasonable to anticipate progress in learning the biology and planning the suppression of snipeflies.

In the main, the most harmful Alaskan mosquitoes worthy of special suppression measures include *A. punctor* forms, *communis*, *impiger*, *excrucians*, *fitchii*, *intrudens*, *diantaeus*, and *C. impatiens* and *C. alaskaensis*. It is difficult to be objective quantitatively about culicine larval populations; the common forms are usually listed for the sake of completeness from a wide variety of marginal atypical habitats. However, only favorable habitats, where a species is so abundant as to cause concern, ought to be considered typical. By reasoning so, at any rate, it has been possible for entomologists to characterize the habitat of each Alaskan mosquito, for all practical purposes. Several representative examples of Alaskan mosquito habitats have been described in detail elsewhere (*11–13*).

Quaking Bogs

Public Health Service entomologists have shown that *Drepanocladus-Carex* quaking bogs are the preferred larval habitat of only one Alaskan *Aedes* (*11*). In his northern Michigan sphagnum mat-mosquito study, Irwin (*12*) reported a perplexing wiggler resembling *A. diantaeus*. The new species was described by Smith (*13*), who discovered it in a Massachusetts quaking bog, and named *Aedes pseudodiantaeus* (now called *Aedes decticus*). It is now practicable to study the biology of *A. decticus* where it abounds in Alaskan quaking bogs.

Permanent and Semipermanent Waters

The characteristic mosquitoes of weedy lakeshores and permanent ponds in Alaska are *Anopheles* and *Culex*. Their specific environmental requirements differ markedly, nevertheless. The sun-loving *Anopheles* occurs in the open, and especially in warmer water than the shade-loving *Culex* which hides in clumps of *Carex* and other sedges.

Dystrophic ponds within bogs are the preferred habitat of *C. impatiens* and *C. alaskaensis*. However, the *C. impatiens* female deposits her raft freely on the open water of weedless basins whereas *C. alaskaensis* oviposits chiefly within dense clumps of dead *Carex*. Consequently it is feasible to predict, in regions where

both species occur, which larva will predominate in a particular pond. *Culiseta morsitans* also breeds in pondlike bog inclusions but primarily in senescent bogs of the *Sphagnum-Ledum-Picea* class which are choked with *Myrica gale* or *Carex*.

Tundras

In the boggy pools of the vast arctic and subarctic tundra waterscapes, there develop distinct tundra varieties of two species of the *A. punctor* complex. Whatever the taxonomic category to which these perplexing varieties are assigned, they certainly constitute major pests. It was recently shown (*14*) that the *A. communis* form, breeding in the brushy inclusions of the tundra and alpine meadows, manifests habits not typical of the species. The males are able to swarm for mating in the open treeless wastes even though *A. communis* is typically a "woods" mosquito swarming only in deep shade. Possibly this open-country form should be considered a tundra variety of *A. communis*.

Salt Marshes

Alaska has an important salt marsh mosquito pest which belongs to the *A. punctor* complex like the principal tundra pests. It breeds in myriads in arctic, subarctic, and temperate brackish coastal marshes. Dyar designated this form *A. punctodes*, and it may be necessary to restore its specific standing when the puzzling *A. punctor* complex becomes better understood. At any rate, the basic knowledge of its biology for settling academic questions and undertaking practical control of salt marsh mosquitoes is now being acquired (*15*).

Summary

Certain general correlations of life cycle with cold-tolerant stages and geographic distribution of mosquitoes in Alaska have been noted. Similarly, there is correlation of habitats with type of cycle. The species belonging to the *Aedes cinereus* cycle breed in temporary waters or the drying margins of semipermanent waters. The earlier species develop in snow water retained by the underlying frost. The later species require water which persists longer. Species of the *Culiseta impatiens* cycle, however, occur only in permanent waters or the most persistent residual pools of semipermanent waters. There are no Alaskan species known to breed normally either in artificial containers such as tin cans or in treeholes, the water of pitcher plants, or other small collections of water.

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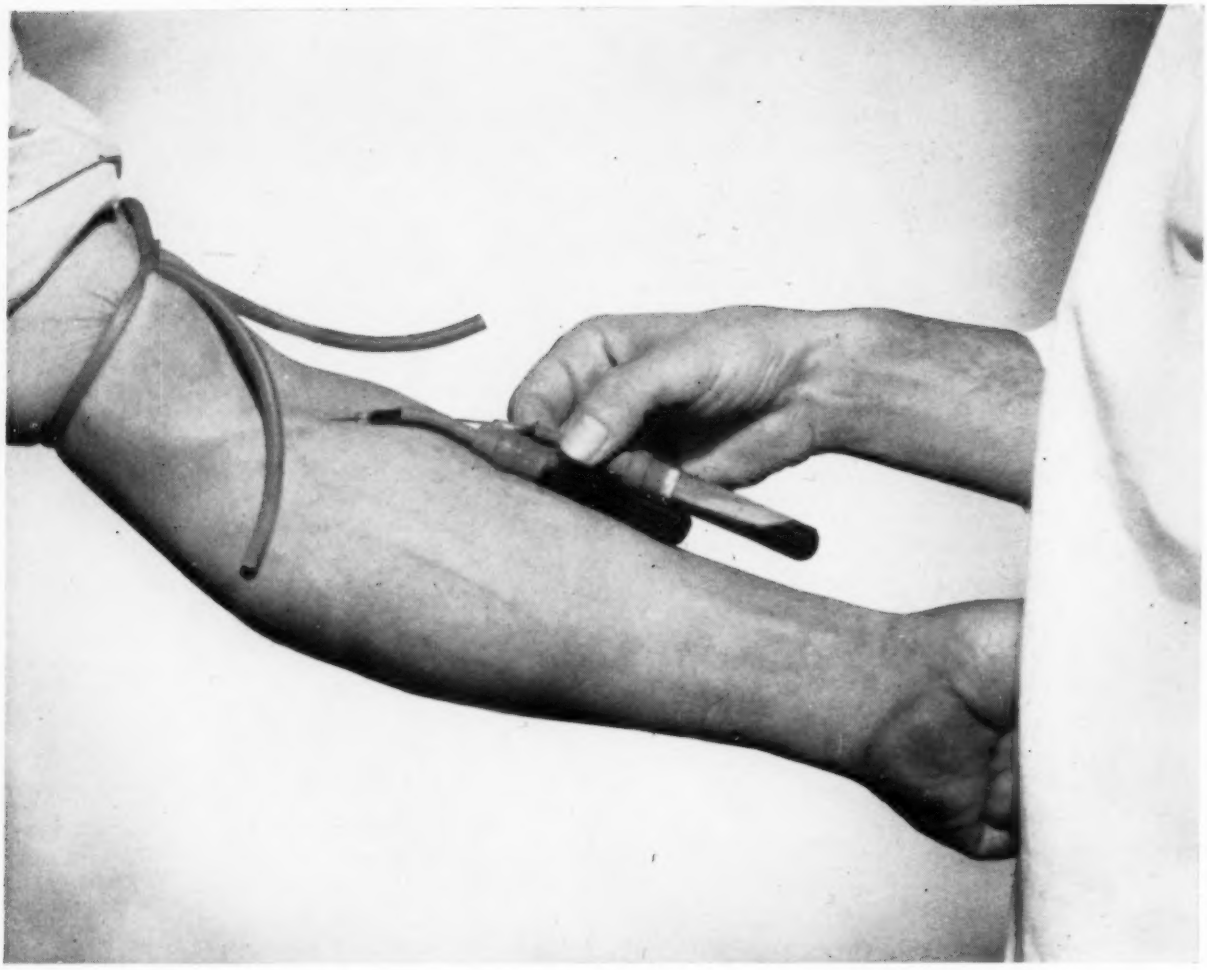


idea

Piggyback Blood Testing

The Sheppard vacuum-packed blood-testing tube has been used in mass blood-testing programs by many State, county, and city venereal disease programs for the past 5 to 7 years.

The Sheppard tube proved to be a valuable aid to the speed and efficacy of mass blood testing. Occasionally, however, a tube with a faulty vacuum would fail to draw blood, necessitating a second attempt.

Survey workers using the tubes readily developed the technique of leaving the first needle in the vein and inserting the needle of a second tube into the rubber sleeve of the first, releasing the vacuum and drawing blood into the second tube via the first tube, thereby avoiding a second venipuncture.

The picture above, taken by Dr. Charles M. Cameron, Jr., of the University of North Carolina School of Public Health, shows blood specimens being taken in this manner during the Cherokee Indian Reservation multiphasic survey conducted by the North Carolina State Board of Health in April 1955.

As a result of this experience in the piggyback method of blood drawing, the District of Columbia Department of Public Health has combined both syphilis and diabetes detection in a mass blood-testing program.

Prepacking the second tube with 30 milligrams of sodium fluoride is the only special preparation required for the dual testing. The sodium fluoride acts as a sufficient anticoagulant for 3 cubic centimeters of blood and allows refrigeration storage of the specimen until it reaches the laboratory.

The piggyback blood-testing method was introduced in Washington, D. C., in June 1955 in a house-to-house blood-testing survey. The reaction of the public was, "Two tests for the pain of one is only half bad."

—JOHN L. PENDLETON, *U. S. public health representative*
District of Columbia, Department of Public Health.

Conference Report

no single blueprint but a common pattern . . .

FOR COMMUNITY ORGANIZATION OF HEALTH SERVICES

AT the annual meeting of the National Advisory Committee on Local Health Departments, sponsored by the National Health Council, the experience of five counties in improving their health facilities illustrated the value of broad citizenship participation in advance planning—for necessary legislative action, for intensive education of the voter, and for continued maintenance of public interest in the operation of established programs.

The meeting in New York City, February 1, 1956, discussed ways of achieving community organization for improving existing health services. Speakers outlined the history of community efforts in Erie County, Pa., Burlington County, N. J., Jackson County, Ohio, Woodford County, Ky., and Saline County, Kans. The 1956 meeting was the third in a series of annual discussions on the problems of development and maintenance of local health services. The two earlier sessions were devoted to the problems of local financing and to community attitudes toward local health services.

In reviewing the committee's 8-year history, Sherwood A. Messner, chairman, traced a trend toward experimentation in health department organization. He pointed to the growing recognition that a single blueprint is not suitable for organizing health department services. Since 1945, 40 city-county health departments have been organized in 16 States. Other States have developed multicounty districts. Some States are following the traditional pattern of a health department for each county. Today there are 1,442 local health units in the Nation.

Close to 100 representatives of national health, welfare, and civic organizations and official agencies took part in the one-day program.

Discussion brought out that the successful attempt for improving local health services has involved as many citizens as possible in preliminary fact-finding surveys of community needs as well as in the planning of subsequent publicity campaigns; that the support of every community group which might be even remotely concerned should be solicited; that timing of publicity is critical; and that, in general, campaigns should be short and intensive, leading immediately to the ballot box, if voter approval is necessary. Financing of health services appeared to be a minor problem once strong community organizations were actively involved.

Build With Voluntary Groups

"We can afford good local health services if only we want them," A. L. Chapman, M.D., medical director, Region II (New York City), Public Health Service, told the meeting.

Dr. Chapman said that people are more interested in supporting "health services" for which they feel a need than in supporting "health departments," about which they know too little. Because modern health services are difficult for the general public to understand, special efforts by community organizations are needed for interpretation of the department's complex activities.

Voluntary groups can be won to support of the health department by helping to develop services in which they have special interest, Dr. Chapman continued. The local health officer must have a talent for organization plus the

ability to educate in the broadest sense and a working knowledge of motivation techniques in order both to gain and then to keep community support, he added.

The importance of building on existing interests which the public already has in health was stressed by other speakers. Discussants agreed that it was vital to maintain public support of the health department after its establishment. Use of a citizens committee to which the department would report annually and publicity about the department's activities in the local press were two of the methods suggested for holding public interest.

Community Organization Vignettes

Case histories of the five counties revealed a common pattern of community organization even if no single blueprint was followed.

Erie County

Erie County, Pa., where voters in November 1955 approved provisions for a county health department, was represented by Russell B. Roth, M.D., chairman of the new county board of health and former president of the Erie County Medical Society. He told how an intensive publicity campaign put strong emphasis on informing the voters.

A speakers bureau in the Erie County Health Council, which organized and conducted the campaign, used dramatic examples with emotional appeal in talks before all possible local groups.

Dr. Roth emphasized the importance of enlisting the cooperation of trusted community leaders. He stressed the need for factual material pointing up deficiencies in public health.

Burlington County

Jesses B. Aronson, M.D., district health officer, Central State Health District, New Jersey Department of Health, told how Burlington County, N. J., obtained county nursing services despite community apathy toward improving health services.

With the formation of a citizens group representing voluntary health and welfare agencies, the medical society, local boards of health, labor organizations, and civic and professional groups, and with the advice and assistance of the State health department, the Burlington County Public Health Nursing Association was brought into being. The association is a voluntary one, partly subsidized by official agencies.

The eventual goal, Dr. Aronson said, is a health department to serve the entire county.

Jackson County

A volunteer group spearheaded the successful effort to win voter approval of a tax levy to pay for a countywide health department in Jackson County, Ohio. The group conducted a 5-week information campaign, relying heavily on an active speakers bureau, newspapers, and radio.

Stating that too few local medical practitioners participated in the campaign, Mrs. John T. Sellers, vice president of the new Jackson County Board of Health and a director of the Jackson County Tuberculosis Association, questioned whether medical students are receiving an adequate understanding of public health.

Mrs. Sellers pointed to the important work done by local units of national voluntary organizations in surveying the community. Valuable assistance also came from the Ohio State Board of Health. Discussants of her talk suggested that field personnel of national agencies can emphasize to their affiliates the importance of working for local health services. Subsequent suggestions mentioned the possibility of asking affiliated agencies to report such activities in their annual reports to national headquarters.

Woodford County

Woodford was the last of Kentucky's 120 counties to install a full-time health department. A 65-year struggle by women's clubs to obtain adequate health services in Kentucky was described by Mrs. Sam Flowers, president of the Kentucky Federation of Women's Clubs.

Mrs. Flowers told how speakers appealed for support of the proposed facility at meetings of all possible groups in Woodford County. A citizens health committee was organized and included a planning board which represented all civic organizations. A photographic survey of insanitary health conditions, views of

outdoor privies, and pictures of dirty restaurants were published in the newspapers. Help was given by the Kentucky State Department of Health and by the medical profession. The measure for the new health department failed to pass the fiscal court when first presented but was successful in 1955.

Saline County

After 33 years of frustration, Saline County, Kans., also achieved success in 1955, when community interest in a mental health guidance center sparked the establishment of a countywide health department. Henry C. Huntley, M.D., assistant medical director, Region II (New York City), Public Health Service, reported Saline County's earlier attempts to achieve a county health setup.

Three Basic Steps

In summing up the group reports, buzz sessions, and discussion periods, Erval R. Coffey, M.D., health officer of Greenwich, Conn., listed three basic steps in sustaining health services:

- Learn the facts about the community and deliver the facts to the public.
- Enlist all groups in the community in the improvement drive.
- Maintain public interest after the initial victory.

The Bulletin on Local Health Units carried a story of the annual meeting in the January–February 1956 issue. The bulletin is published by the National Advisory Committee on Local Health Departments, National Health Council, 1790 Broadway, New York 19, N. Y.

technical publications

The National Cancer Institute

Public Health Service Publication No. 458. 1955. 22 pages; illustrated. 20 cents.

This brochure gives a concise history of the National Cancer Institute of the Public Health Service.

A short review of the present status of the cancer problem is followed by an illustrated account of what the institute is doing—in research, in training, and in control—to help solve the problem of cancer.

About 70 percent of the annual appropriation for the various activities of the institute is devoted to cancer research, and more than two-thirds of the funds are granted to scientists in non-Federal institutions such as universities and hospitals. Other grant categories discussed include financial support for cancer teaching in medical and dental schools, programs designed to aid young physicians and scientists specializing in cancer work, grants to State health agencies, and field investigation grants directed toward the support of such projects as studies of the incidence of cancer in relation to certain environmental factors.

Discussed are methods used to acquaint practicing physicians and dentists with new developments in the cancer field, consultation services to State health agencies, public health educational programs, the radium loan program, and cooperation with voluntary health agencies interested in the cancer problem.

Reported Tuberculosis Data Calendar Year 1954

Public Health Service Publication No. 471. 1955. 29 pages. 25 cents.

Data are presented for newly reported tuberculosis cases for the United States and each State by source of morbidity report, activity status, form and extent of the disease, race, sex, and age. Data on X-ray case-finding activities, mortality, and public health nursing visits are also included.

Reports were received from all the States, the District of Columbia, Alaska, Hawaii, and Puerto Rico. An analysis of each table summarizes data for the years 1952, 1953, and 1954 and points out pertinent characteristics inherent in the data.

This section carries announcements of all new Public Health Service publications and of selected new publications on health topics prepared by other Federal Government agencies.

Publications for which prices are quoted are for sale by the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. Orders should be accompanied by cash, check, or money order and should fully identify the publication. Public Health Service publications which do not carry price quotations, as well as single sample copies of those for which prices are shown, can be obtained without charge from the Public Inquiries Branch, Public Health Service, Washington 25, D. C.

The Public Health Service does not supply publications issued by other agencies.

A preliminary report of a longitudinal study begun in 1952 on the epidemiology of oral health in children, covering periodontal and systemic conditions, as well as caries.

Oral Health Study in Children of Suburban Washington, D. C.

By A. L. RUSSELL, D.D.S., M.P.H.

THIS is a preliminary report on a study of oral health in a population of children as the population becomes progressively less susceptible to dental caries following fluoridation of its community water. The study is not designed as a test of the fluoride-dental caries relationship; the study plan assumes that this relationship is fully established and that a progressive inhibition of dental caries will, in fact, occur. The study's broad and long-term objectives are to augment the descriptive epidemiology of dental caries and to lay a foundation for a descriptive epidemiology of periodontal disease as it first appears in relatively young persons. In addition the study group has been and will be utilized, as a population of known status and background, for short-term observation of pertinent phenomena. Two such reports, based in part upon this population, have already been published (*1*, *2*).

The present report is limited to observations on dental caries. It describes the study population, criteria and methods of examination, and the status of the group at the time of first examination in 1952 and includes summary data from examinations in 1953 and 1954. Evidence is presented to support other findings that an inhibition of dental caries in children will follow use of a fluoridated domestic water. The continuing study is being conducted by the National Institute of Dental Research, Public Health Service, in Prince Georges and Montgomery Counties, Md., two counties adjacent to the District of Columbia.

Dr. Russell is chief, Epidemiology and Biometry Branch, National Institute of Dental Research, National Institutes of Health, Public Health Service, Bethesda, Md.

The Study Situation

The population of Montgomery County in 1950 numbered 164,401 persons of whom 93.6 percent were white. The population of Prince Georges County was 194,182 persons, 88.2 percent of whom were white.

Both counties are predominantly urban. Only 6.4 percent and 5.9 percent of the residents of the respective counties lived on farms in 1950. The median number of school years completed by persons 25 years of age or older was 12.6 in Montgomery County and 12.0 in Prince Georges County. Median family income was $4,532 in the one county and $3,634 in the other (*3a*). The median value of one-family homes was $16,136 in Montgomery County and $11,696 in Prince Georges County (*3b*). Principal sources of income were Federal employment, wholesale and retail trade, construction, and service occupations. Only about 10 percent of

the population were employed in manufacturing (*4*).

Compared with the United States as a whole, residents of the two counties had completed more schooling, had earned higher incomes, and had lived in more expensive homes. For the entire Nation, the median number of school years completed in 1950, by persons 25 years of age or older, was 9.3 years (*5a*). Median incomes were $2,970 for urban families, and $2,186 for rural nonfarm families, respectively (*5b*). And the median value of a one-family home, in urban and rural nonfarm areas, was $7,354 (*5c*).

About 5,000 elementary and junior high school pupils have been examined annually since the oral health study began. The Montgomery County group is taken from an area centering around the Takoma Park Junior High School, adjacent to the District of Columbia across its northeast border. The Prince Georges County group lives in the general vicinity of the Maryland Park and Suitland Junior High Schools, near the southeast border of the District. These areas were chosen as representative of suburban Washington from the socioeconomic standpoint and because their residents have been relatively nonmigratory.

Detailed data concerning the number of topical sodium fluoride treatments were obtained for each child through a schedule completed and returned by his parents. The proportion of treated children was so high in one Montgomery County neighborhood that it seemed prudent to exclude this entire group in computing caries and eruption expectancy tables.

Data for eight schools were analyzed separately by age, sex, and school. Though the proportion of filled teeth to total caries experience was uniformly higher in Montgomery than in Prince Georges County children, all children in the study seemed to have been drawn from the same universe as regards total caries experience in deciduous and permanent teeth and in eruption of permanent teeth and, hence, were combined into one single group for study.

Children in the study group are furnished a fluoridated water by the Washington Suburban Sanitary Commission although at the outset of the study one small group in Prince Georges County used water from wells. Raw water is taken from the Patuxent River and from the northwest branch of the Anacostia River. The two watersheds drain about 105 square miles to the north and east of the District of Columbia. The raw water receives similar treatment in two processing plants. Treatment includes aeration, prechlorination, flocculation, rapid sand filtration, adjustment of alkalinity with hydrated lime, postchlorination, and the addition of fluoride as sodium fluosilicate by means of dry feeders. With the exception of fluoridation these procedures have been uniform throughout the lives of the children under study. Tap water prior to 1952 was essentially fluoride free.

The fluoride feeders were started on December 28, 1951. During a period of preliminary adjustment, operation was not continuous. For this reason and because of the reservoir of fluoride-free water stored in the system of mains, a fully fluoridated water was not available at all taps throughout the distribution system until the last week of February in 1952. From that time onward, spot tap fluoride determinations carried out by the Washington Suburban Sanitary Commission have been faithful reflections of the daily fluoride levels in finished water at the filtration plants with the exception of a short period in mid-June 1952, when water in the Prince Georges County area was diluted with fluoride-free water obtained through a cross connection with the District of Columbia supply. During that period the fluoride level in the Suitland area dropped to 0.50 p.p.m. F. The District of Columbia supply has since been fluoridated. The average daily fluoride content of finished water at the Robert B. Morse filtration plant, serving generally the Montgomery County study children, was 0.98 p.p.m. F in 1952 and 0.94 p.p.m. F in 1953. The average daily fluoride content of finished water at the Patuxent filtration plant, serving generally the Prince Georges County study children, was 0.90 p.p.m. F over both years.

Methods and Criteria

All examinations have been carried out by dental officers of the National Institute of Dental Research. Mouth mirror and explorer are employed, with the child seated in a portable dental chair, under a portable examination

light. Examination results are dictated to a recorder in a code similar to that suggested by Klein and Palmer (*6*). Some changes have been made in the code to avoid phonetic confusion and to permit the separate notation of pit-and-fissure or smooth-surface carious lesions found on a single tooth surface. Examinations are scheduled so that each child is observed during the same calendar week on successive years.

All criteria are designed to assure the highest practicable degree of comparability among examiners:

None but positive lesions which admit the explorer point are recorded as carious.

Decalcified areas in the gingival third of the labial or buccal surfaces and opacities of marginal ridges which suggest a possible proximal lesion are recorded as questionable and tabulated as normal unless a definite enamel discontinuity is demonstrated with the explorer.

Deep pits and fissures are similarly recorded as questionable unless softened dentin is encountered by the explorer point or there is visible evidence of backward decay at the dentinoenamel junction.

A tooth is considered to be in eruption if any portion protrudes through the gum.

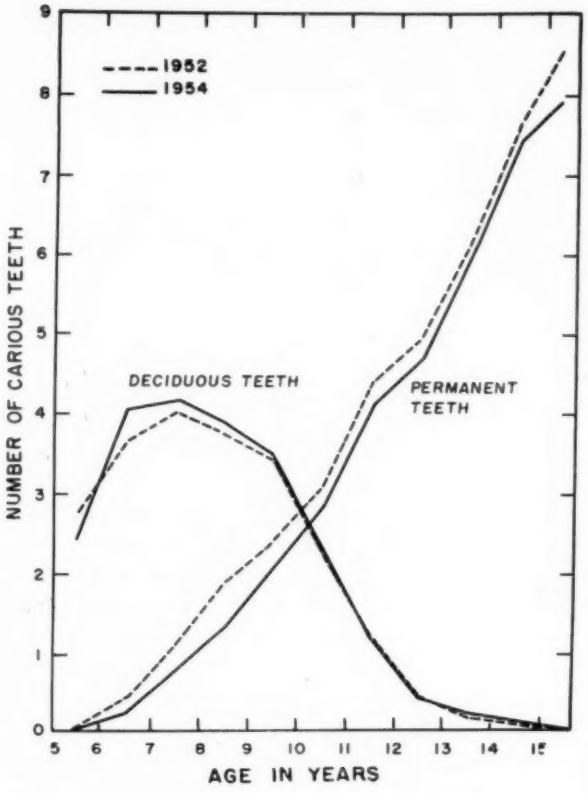
Criteria for the scoring of periodontal disease have been discussed in detail in an earlier report (*7*).

Initial Status

A total of 4,737 white children aged 5 through 15 years were examined between December 1951 and February 1952, coincident with the fluoridation of the water supply. The dental caries experience of this group of children is summarized in table 1.

Subsequent study of history records supplied by parents disclosed that 1,950 of these children had been born in and had been continuous residents of the area, except for short vacation trips in some instances, and had not received any treatment designed to prevent dental caries. Findings for this group, designated hereafter as the baseline population, were accepted as representative for children in the general area in the absence of a known caries-

1952 and 1954 caries experience of continuous-residence children of Montgomery and Prince Georges Counties, Md., who had not received caries prevention treatments.



inhibitory factor and were utilized in the construction of a family of expectancy curves for caries increments in teeth and tooth surfaces, the eruption of permanent teeth, and the exuviation of deciduous teeth. Oral findings for these children are presented in broad outline in table 2.

The general caries experience in the baseline group is considerably lower than it was in children examined initially at Grand Rapids (*8*), and it was somewhat below the caries levels reported at the beginning of the Newburgh and Brantford studies (*9*, *10*). Very similar findings were returned by Arnold and McClure (*11*) in a study of children aged 12 and 13 years in 1939 and 1940 in Arlington, Va., another suburb of Washington, D. C., and by the Southern Maryland District Dental Society, which examined about 15,000 other children in Montgomery and Prince Georges Counties early in 1952. The findings for this separate group of children are summarized in table 3.

On the basis of these comparisons, the mean number of decayed, missing, or filled (DMF) permanent teeth in baseline children aged 11 years appears to be somewhat high. If this is true, computations of yearly caries increment based on these data will overestimate the true increment between the ages of 10 and 11 years and will underestimate the true increment between the ages of 11 and 12 years.

Table 4 shows crude caries rates for children, comparable with the baseline group, who were observed in 1952, 1953, and 1954. Findings for caries in permanent teeth in 1953, after 1 year of fluoridation, are in general slightly higher than the findings for the baseline year though the differences are well within the range of chance variation. This has been a common phenomenon in fluoridation studies where examinations are carried out with mirror and explorer. Reported DMF means were somewhat

Table 1. Oral status of 4,737 children in Montgomery and Prince Georges Counties, Md., 1952

Mean age (years)	Number of children	Mean number of permanent teeth		Mean number of deciduous teeth		Percent of caries-free children	
		In eruption	DMF [1]	Present	def [2]	Permanent dentition	Deciduous dentition
5.44	186	1. 08	0. 03	19. 19	2. 15	97. 3	47. 3
6.47	416	5. 34	. 30	16. 22	3. 16	86. 1	33. 7
7.45	487	9. 14	. 96	13. 30	3. 50	56. 7	28. 1
8.49	475	11. 73	1. 74	11. 17	3. 56	36. 2	21. 1
9.48	499	14. 21	2. 46	8. 80	3. 45	22. 6	20. 6
10.47	394	17. 99	2. 94	5. 58	2. 35	19. 0	34. 0
11.51	420	22. 26	4. 01	2. 74	1. 27	11. 7	54. 8
12.53	601	25. 45	4. 88	1. 05	. 52	9. 0	75. 7
13.50	572	27. 09	6. 29	. 35	. 19	7. 2	89. 0
14.49	513	27. 53	7. 86	. 14	. 05	3. 9	95. 9
15.37	174	27. 67	8. 63	. 02	. 02	4. 0	98. 3
All children—10.64	4, 737	18. 09	3. 71	6. 49	1. 84	28. 4	54. 0

[1] Decayed, missing, or filled.
[2] Decayed, extraction indicated, or filled.

Table 2. Oral status of 1,950 continuous-residence children in Montgomery and Prince Georges Counties, Md., who, on initial examination in 1952, had not had topical fluoride or other caries-preventive treatments

Mean age (years)	Number of children	Mean number of permanent teeth		Mean number of deciduous teeth		Percent of caries-free children	
		In eruption	DMF [1]	Present	def [2]	Permanent dentition	Deciduous dentition
5.44	60	1. 40	0. 03	19. 10	2. 77	98. 3	36. 7
6.46	171	5. 63	. 41	16. 04	3. 67	81. 3	26. 9
7.45	211	9. 22	1. 09	13. 20	4. 04	50. 7	22. 3
8.50	181	11. 59	1. 90	11. 27	3. 78	32. 6	14. 9
9.47	223	13. 97	2. 42	9. 07	3. 43	19. 7	18. 4
10.47	199	18. 28	3. 09	5. 32	2. 30	16. 6	33. 7
11.50	191	22. 47	4. 39	2. 59	1. 29	12. 6	52. 4
12.54	228	25. 48	4. 96	1. 03	. 47	8. 3	77. 2
13.51	233	27. 05	6. 15	. 32	. 16	6. 9	91. 0
14.50	188	27. 56	7. 66	. 18	. 07	3. 7	94. 1
15.36	65	27. 80	8. 57	. 00	. 00	7. 7	100. 0
All children—10.60	1, 950	18. 07	3. 69	6. 49	2. 03	26. 3	50. 3

[1] Decayed, missing, or filled.
[2] Decayed, extraction indicated, or filled.

higher after 1 year of fluoridation at Grand Rapids and Brantford (*8, 10*). The effect is specifically graphed, for first molars, in the third-year report from the Newburgh-Kingston study (*12*).

Table 3. Mean numbers of decayed, missing, or filled permanent teeth reported for 14,936 white children in Montgomery and Prince Georges Counties, 1952 [1]

Age last birthday	Number of children examined	Mean number of DMF [2] teeth
5	409	0.04
6	1,360	.34
7	1,389	1.08
8	1,428	1.78
9	1,333	2.44
10	1,167	3.19
11	1,059	3.79
12	1,260	5.10
13	1,145	6.36
14	1,150	7.80
15	1,238	8.83
16	1,057	10.68
17	811	11.68
18	117	10.68
19	12	15.33
20	1	7.00

[1] From unpublished data reported by Southern Maryland District Dental Society to Public Health Service Region III (Washington, D. C.).
[2] Decayed, missing, or filled.

Lesions detected for the first time by mirror and explorer, after 1 year of fluoridation, are mostly lesions which began before fluoridation was instituted. By the end of the second year, however, it may be assumed that the majority of lesions detected for the first time by the explorer had their inception after fluoridation began. In the present study population, the second postfluoridation examination shows a drop in total numbers of decayed, filled, or missing permanent teeth, a drop averaging 0.27 teeth per child. Mean numbers of deciduous teeth which are decayed, filled, or indicated for extraction (def) are unchanged or slightly higher.

Mean caries data for the baseline children examined in 1952 and for comparable children examined in 1954 after 2 years of fluoridation are illustrated in the accompanying chart.

Increments of New DMF Teeth

Expectancy increments of newly decayed, missing, or filled permanent teeth over a period of 1 year were computed for each age group, by the method used in the Hagerstown studies (*13*), from findings for the 1952 baseline group. Baseline children aged 7 years, for example, had an average of 1.090 decayed, missing, or filled permanent teeth. Six-year-old children

Table 4. Summary of findings for continuous-residence children in Montgomery and Prince Georges Counties, Md., who used city water, had not received topical fluoride or other caries-preventive treatments, and were examined in 1952, 1953, and 1954

Age last birthday	Number of children examined			Mean number of DMF [1] teeth				Mean number of def [2] teeth			
	1952	1953	1954	1952	1953	1954	Difference, 1952 and 1954	1952	1953	1954	Difference, 1952 and 1954
5	60	67	94	0.03	0.02	0.01	−0.02	2.77	2.06	2.49	−0.28
6	171	238	306	.41	.32	.22	−.19	3.67	4.05	4.07	+.40
7	211	175	268	1.09	1.01	.80	−.29	4.04	3.95	4.19	+.15
8	181	192	189	1.90	1.63	1.37	−.53	3.78	3.93	3.91	+.13
9	223	175	192	2.42	2.43	2.08	−.34	3.43	3.36	3.52	+.09
10	199	210	190	3.09	3.01	2.86	−.23	2.30	2.41	2.33	+.03
11	191	181	204	4.39	3.82	4.11	−.28	1.29	1.11	1.25	−.04
12	228	245	279	4.96	5.13	4.70	−.26	.47	.68	.44	−.03
13	233	252	284	6.15	6.65	5.99	−.16	.16	.23	.23	+.07
14	188	287	249	7.66	8.35	7.43	−.23	.07	.07	.12	+.05
15	65	119	116	8.57	9.62	7.92	−.65	.00	.04	.03	+.03
All children	1,950	2,141	2,371	3.69	4.11	3.42	−.27	2.03	1.91	2.08	+.05

[1] Decayed, missing, or filled.
[2] Decayed, extraction indicated, or filled.

had an average of 0.409 decayed, missing, or filled permanent teeth. The difference between these two findings, 0.681 teeth, was accepted as the expected average increase in carious permanent teeth as a group of children goes from the age of about 6½ to about 7½ years. Similar computations yielded the array of expected yearly caries increments shown in table 5.

Among comparable children examined in 1954, there were 1,218 aged 6 through 15 years who had also been examined in 1953. By matching 1953 and 1954 examination records for each of these children, actual numbers of newly carious permanent teeth were determined and analyzed as mean changes over the 12-month period. This method permitted the computation of standard error for each mean change and estimation of the probability that any observed increment varied only by chance from the absolute expectancies computed from the 1952 data. These analyses are also summarized in table 5.

If the presumptive 1952 increment rates had obtained throughout the year 1953–54, 1,130 newly carious permanent teeth would have developed in the group, or an average of 0.928 tooth per child. The actual increment was 910 newly carious permanent teeth, or an average of 0.747 per child—a difference of 19.5 percent. It is highly improbable that this difference of almost 20 percent is due to chance variation.

About the same result is obtained if expectancy increments are based upon the independent examination conducted by the Southern Maryland District Dental Society. From their data, 1,146 newly carious permanent teeth would have been predicted for the study children during the 1953–54 school year, a difference of 20.6 percent.

Discussion

Comparisons of observed increments with expected increments, as computed from the 1952 baseline data, should be interpreted with caution. Each of the age groups in the 1952 data is an independent group, subject to biological variation. In the baseline array, DMF totals for children aged 11 years seem rather high. If this be true, the expected increment is an overestimate of DMF incidence between ages 10 and 11 and an underestimate of DMF incidence between ages 11 and 12. This factor of variation is present to a greater or lesser degree throughout the array. Little reliance, then, should be placed on the comparison of expected

Table 5. Increments of new decayed, missing, or filled permanent teeth over 12 months, from 1953 to 1954, in continuous residents of Montgomery and Prince Georges Counties, Md., who were examined in both years, used city water, and had not received topical fluoride or other caries-preventive treatments, as compared with increments computed from data for comparable children of the same counties in 1952

Expected mean DMF [1] increment, past year	Children examined in 1953 and again in 1954				
	Mean age, 1954	Number examined	Actual mean DMF [1] increment, 1953–54	Difference between actual and expected increments	Probability difference due to chance [2]
0.376	6. 63	27	0. 111 ± 0. 082	−0. 265	< 0. 001
0.681	7. 51	160	. 425 ± . 070	− . 256	< . 001
0.811	8. 45	121	. 736 ± . 102	− . 075	. 23
0.516	9. 47	137	. 489 ± . 097	− . 027	. 39
0.668	10. 51	120	. 758 ± . 120	+ . 090	. 23
1.302	11. 45	133	1. 075 ± . 132	− . 227	. 04
0.569	12. 47	106	. 840 ± . 156	+ . 271	. 04
1.194	13. 53	175	1. 006 ± . 151	− . 188	. 11
1.510	14. 49	171	. 947 ± . 176	− . 563	< . 001
0.909	15. 39	68	. 324 ± . 267	− . 585	. 01
0.928		1, 218	. 747 ± . 046	− . 181	< . 001

[1] Decayed, missing, or filled.
[2] Based on areas under the normal curve.

with observed increment in any specific age group. The study plan intends that age-specific incidence data shall ultimately be shown as trends, valid in themselves, with expectancy values serving only as points of departure.

On the other hand, age-specific error tends to be random, and overestimation at one age tends to cancel out underestimation at another if the entire group is considered as a unit. This is well illustrated by the close agreement between expectancy data calculated from the two independent examinations cited. No matter which one of these expectancy curves is used, the same conclusions are reached: that about 20 percent fewer permanent teeth became carious in the whole group than would have been expected on the basis of the 1952 examination and that it is highly improbable the difference is due to chance.

This particular method is not appropriate at all when applied to deciduous teeth without any means of determining whether a missing deciduous tooth has been lost prematurely or normally. On the basis of the cumulative totals shown in table 4, no change in the prevalence of caries in deciduous teeth is apparent in these study groups. Deciduous teeth in these children had been in eruption and at risk of caries for 3 years or more at the time the water supply was fluoridated.

Summary

This preliminary report has described the examination criteria for dental caries and methods in use and has defined the population under observation in a continuing study of oral health in elementary and junior high school children of Montgomery and Prince Georges Counties, Md. The two counties are adjacent to the District of Columbia. The domestic water used by these children was fluoridated with sodium fluosilicate late in December of 1951. Evidence is presented that there was a statistically valid decrease of roughly 20 percent in the number of permanent teeth becoming carious during the second year of fluoridation, judged by findings from the baseline examination early in 1952.

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